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CANCER AND OTHER HUMAN DISEASES: DOE RESEARCH PROGRAMS

HEARINGS

BEFORE THE

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

OF THE

COMMITTEE ON SCIENCE AND TECHNOLOGY U.S. HOUSE OF REPRESENTATIVES

NINETY-EIGHTH CONGRESS

SECOND SESSION

MARCH 6, 13, 1984

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CANCER AND OTHER HUMAN DISEASES: DOE RESEARCH PROGRAMS

TUESDAY, MARCH 6, 1984

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE
RESEARCH AND ENVIRONMENT,
Washington, DC.

The subcommittee met, pursuant to notice, at 2 p.m., in room 2325, Rayburn House Office Building, Hon. James H. Scheuer (chairman of the subcommittee) presiding.

Present: Representatives Scheuer and Schneider.

Mr. SCHEUER. The Subcommittee on Natural Resources, Agriculture Research and Environment will come to order.

One of the major problems facing America today is cancer, which results in the death of 400,000 Americans each year; and it's something which affects almost each and every person in society, and that's the subject of today's hearing.

I would ask unanimous consent for my opening statement to be placed in the record so that we can get on with the witnesses whom we need to hear.

[The opening statement of Mr. Scheuer follows:]

OPENING STATEMENT OF
JAMES H. SCHEUER
MARCH 6, 1984

THE SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT WILL COME TO ORDER.

ONE OF THE MAJOR HEALTH PROBLEMS FACING AMERICA IS CANCER WHICH RESULTS IN THE DEATH OF OVER 400,000 AMERICANS EACH YEAR.

THE DEPARTMENT OF ENERGY (DOE) HAS A MAJOR RESEARCH EFFORT UNDERWAY TO DETERMINE WHETHER EXPOSURE OF HUMANS TO RADIATION AND CHEMICALS ASSOCIATED WITH ENERGY PRODUCTION AND USE RESULTS IN CANCER.

OTHER DOE RESEARCH EFFORTS
FOCUS ON THE USE
OF RADIATION TO
TREAT CANCER.

SINCE CANCER OFTEN DOES
NOT MANIFEST ITSELF
UNTIL YEARS AFTER
EXPOSURE, LONG-TERM
STUDY IS NEEDED.

IN ORDER TO CONDUCT THE
NECESSARY RESEARCH,
A COMMITMENT TO THE
NECESSARY LONG-TERM
FUNDING BY THE
ADMINISTRATION IS
ALSO MANDATORY.

PAST ADMINISTRATIONS HAVE COMMITED THEMSELVES TO THE SUPPORT OF THE EXCELLENT CANCER RESEARCH PROGRAMS WITHIN THE DEPARTMENT OF ENERGY.

HOWEVER, DESPITE THE IMPORTANCE OF UNDERSTANDING THE CAUSES OF CANCER, WHICH CAN LEAD TO CURES, FUNDING FOR THIS RESEARCH HAS INCREASED ONLY SLIGHTLY IN THE FY 1985 BUDGET REQUEST (FY 1985 $52.4 MILLION, FY 1984 $51.3 MILLION), WHICH IS LESS THAN A COST OF LIVING INCREASE.

THEREFORE, THIS MODEST INCREASE IS NOT SUFFICIENT.

IN FACT, ONE OF THE NATION'S OUTSTANDING CANCER RESEARCH LABS AT THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, (UCLA) IS SCHEDULED TO BE TERMINATED AND WILL RECEIVE NO DOE FUNDS IN FY 1985.

TODAY'S WITNESSES, INCLUDING REPRESENTATIVES FROM UCLA, WILL EXPLAIN SPECIFICALLY HOW THE FY 1985 BUDGET WILL IMPACT ON THE CANCER RESEARCH PROGRAM.

WHILE I APPLAUD EFFORTS TO REDUCE UNNECESSARY AND DUPLICATIVE EFFORTS, MANY OF THE PROPOSED BUDGET CUTS APPEAR TO BE ARBITRARY, EXCESSIVE, AND WITHOUT MERIT.

THE AMERICAN PEOPLE DESERVE TO KNOW WHAT THESE CHEMICALS PRODUCED BY THE VARIOUS ENERGY TECHNOLOGIES, WILL DO TO THEIR HEALTH AND TO THE ENVIRONMENT.

TODAY'S HEARING SHOULD PROVIDE THE SUBCOMMITTEE WITH AN OVERVIEW OF THE DOE'S CANCER RELATED RESEARCH PROGRAM, AND THE IMPACT OF THE ADMINISTRATION'S PROPOSED FY 1985 BUDGET REQUEST.

NOW, I WOULD LIKE TO RECOGNIZE MY DISTINGUISHED COLLEAGUE FROM NEW YORK, THE RANKING MINORITY MEMBER OF THIS SUBCOMMITTEE, MR. MCGRATH, FOR ANY STATEMENT HE MAY WISH TO MAKE.

I WOULD LIKE TO WELCOME OUR WITNESSES TODAY.

WE WILL BEGIN WITH DR. EDWARD ALPEN, OF THE LAWRENCE BERKELEY LABORATORY AND DR. MICHAEL E. PHELPS OF THE UCLA SCHOOL OF MEDICINE.

Mrs. SCHNEIDER. Let me just say that, having been a living example of the benefits of cancer research, having had Hodgkin's disease myself, I am looking forward to see what kinds of advancements we are making and to enthusiastically encourage a more rapid solution to this disease in all of its forms. I am sure looking forward to this hearing.

That's all I have, Mr. Chairman.

Mr. SCHEUER. Very good. Thank you.

All right. We'll move immediately to our first panel. Dr. Edward Alpen of the Lawrence Berkeley Laboratory, in Berkeley, CA, accompanied by Dr. Thomas Hayes and Dr. Michael E. Phelps of the UCLA School of Medicine in Los Angeles. Please come to the table.

Let me say, before we start, that all of your prepared addresses will be printed in full in the record, so what we hope you'll do is chat with us informally. Take 6 or 7 minutes and give us the highlights of your remarks, and then I'm sure we'll have some questions for you.

First we'll take Dr. Alpen.

STATEMENT OF DR. EDWARD ALPEN, DIRECTOR, DONNER LABORATORY, BIOMEDICAL RESEARCH DIVISION, LAWRENCE BERKELEY LABORATORY, BERKELEY, CA, ACCOMPANIED BY DR. THOMAS HAYES

Dr. ALPEN. Mr. Chairman, members of the subcommittee, thank you very much for allowing us to be here today to give you our points of view on where the cancer——

Mr. SCHEUER. Let me make one thing clear. We didn't allow anybody; we invited you to honor us by appearing. You are aiding us in meeting our mission of legislating for the American people. You

honor us and you honor yourselves by participating in the process. We very much appreciate your coming here. I hope no other witness will say anything about our allowing you to be here today. It's a privilege to hear you.

Dr. ALPEN. Thank you very much, sir.

While many cancers can, of course, be successfully treated with conventional methods, as our minority member said a moment ago, a great deal of progress has been made in the control of cancer in the United States——

Mr. SCHEUER. I wonder if you could just push that mike down a little bit. It's a directional mike. Point it right at——

Dr. ALPEN. How is that?

Mr. SCHEUER. That's great.

Dr. ALPEN. For example, among those cancers treated by radiotherapy today, even though the disease is still confined to its organ of origin—in other words, it is locally confined—there are still about 100,000 deaths annually from that cause alone in the United States. It has been known for some time that if we could improve the local control of cancer, cancer within the organ of origin, that we might be able to do this with a higher radiation dose given precisely to the tissue. Also, a considerable advantage could also be gained if the radiation which is used could more effectively kill oxygen starved tumor cells which are resistant to x rays employed in conventional radiotherapy.

In principle then, significant improvement in the local control of cancer can be achieved by two means: first, the more precise delivery of dose to the diseased tissue, and second, by enhanced killing effectiveness for the beam which is used. And I might say in passing, that the second of these procedures, enhanced killing effectiveness for oxygen starved cancer cells, is the basis of the National Neutrol Therapy Program, which is going on at several centers in the United States today. The neutron beams, however, must by their physical nature sacrifice precise dose localization.

As long ago as 1950 Robert Wilson, a physicist at Berkeley, pointed out that there was a special property of charged particles known as the Bragg ionization peak that would make them extremely suitable for the treatment of cancer. The nature of the Bragg ionization peak is that the radiation tends to stop within the organ in which you plan for it to stop; there's little energy deposited on the way in, and none goes beyond the organ in which the radiation is being delivered. X rays, on the other hand, deliver their energy most intensely just on entering the body, and at greater and greater depth less energy remains for deposition in the tumor. Of course, with x rays some fraction of the dose goes beyond the tumor.

Professor Lawrence took up Dr. Wilson's observation as early as 1950 and started with the treatment of the pituitary disease, tumors within the pituitary gland, which is deep within the brain. Close to 800 patients were treated by Dr. Lawrence and his colleagues, and that is one of the great success stories of the early days of this program. The disease control rate with those 800 patients was in excess of 90 percent.

Now, accelerated particles, which we call heavy ions in our daily jargon, are the nuclei of atoms of any mass, stripped of electrons.

Because they are heavy, these particles will only penetrate tissue if their energy or velocity is raised to very high levels in accelerators especially built for that purpose. Research at LBL has already shown that Professor Wilson's predictions were indeed true, and furthermore, that heavy ions have many of the properties of neutrons for killing oxygen starved cells. The strong and comprehensive program in basic radiation biophysics has provided foundation for some rather important recent medical successes, which I'll describe shortly.

Before doing so, however, I wish to make an additional point. The charged particle beams produced at our accelerators in Berkeley are identical with the charged particle radiation fields which are formed in space, and the evaluation of radiation hazards of charged particle beams in space can in fact be evaluated at terrestrial locations only at the Berkeley Bevalac.

In 1974 the Office of Health and Environmental Research and its predecessors agreed after a review by an expert panel to provide support for further evaluation of these charged particles from accelerators for the treatment of human disease. I can now report on some of the major successes for this program.

The pituitary program, as I mentioned earlier, was the pioneering effort of Dr. Lawrence and demonstrated without a doubt the utility of charged particle beams for treatment of pituitary disease. Interestingly enough, we have set aside any further efforts on that particular disease ourselves since we have accomplished our research goals. The treatment is being provided as routine medical care at cyclotrons at Harvard, at Uppsala, Sweden, and in Russia. Some of the newest and most exciting findings I will now describe for you, and there are three of these in particular. The first is the treatment of melanomas in the eye; a melanoma, of course, is the black-pigmented tumor which occurs widely on skin. It exists as a fairly uncommon tumor which grows inside of the eye. There may be a thousand or so cases newly diagnosed of this disease in the United States. The standard treatment has been removal of the eye immediately upon detection of the tumor. We, and our collaborating group at the Harvard MA General Hospital have been treating these eyes with very precisely localized radiation treatment with heavy ion beams. Our success rate in controlling this disease is now well over 90 percent for patients with over 1 year of followup, and I will say that it will probably approach 98 percent as the statistics accumulate. And that, of course, is for a disease for which there is absolutely no other existing control mechanism. Furthermore, vision is retained in the affected eye after treatment, and the patients have the cosmetic advantage and also the treatment advantage.

Mr. SCHEUER. Excuse me for interrupting, but you may have noticed that we have a rollcall vote now; we have about 6 minutes now, so we're going to suspend now for about 10 minutes and catch the rollcall vote, and we'll be right back.

Dr. ALPEN. All right. Thank you, sir.

[Short recess taken.]

Mr. SCHEUER. We'll go ahead.

Dr. ALPEN. Thank you, sir.

Mr. SCHEUER. And we'll ask all the witnesses to try and terminate their testimony at about 6 or 7 minutes, because we're under a little bit of time pressure.

Dr. ALPEN. I understand, sir.

The second group of tumors about which I'm going to speak briefly is tumors of the brain and spinal cord which require very precise dose localization. This is another group of cancers which are in the central nervous system which are so close to critical structures that they can't be treated by normal means. We have treated with heavy ion therapy, now, about 20 of these tumors, of which there are several thousand newly diagnosed each year; and of the 20 we have so far treated, 17 have adequate followup, and we have complete disease control in these 17 patients. We are pleased with that success because these tumors are only rarely successfully treated by conventional radiotherapy or surgery.

And the final very important success I would like to take a moment to tell you about is to talk about arterio-venous malformations in the brain. This is a bit like having a varicose vein deep inside of your brain, which can break. A very large number of people are found to have defects of congenital origin in the circulatory system in the brain, and there are about 10,000 to 20,000 new diagnoses every year in this country. These defects are life threatening; some of them can be treated by standard surgical means, but 2,000 or 3,000 patients per year cannot be. At Berkeley and Harvard these patients are being treated with charged particle beams, and I want to take this time to show you a couple of slides of the results.

In the Berkeley experience well over 50 patients have been treated and none of the 50 patients treated so far have shown any further bleeding. In other words, we have 100-percent disease control in these patients. The slide on the board shows you, in cross-section, a vascular malformation deep in the brain of a patient. The slide—centrally, at the top, with the yellow lines around it—shows the delivery of the dose to that deep arterio-venous malformation in the brain. The cross-section at the right shows the same thing in plane view. As you see, that's a very small lesion which can be only treated by this means, and is not accessible to treatment by any other method.

The next slide will show the results rather graphically on two patients who were treated, and shows the original lesions in these patients below. And that is what an arterio-venous malformation looks like, a big varicose vein deep in the brain, and which can bleed and cause death. Fourteen months after their therapy, the upper two slides show the complete resolution of their vascular structures, back to normal conditions.

May I have the lights again, please?

Of course, we've had some failures as well as successes, and there are some diseases where we've not done any better than conventional therapy, and I would particularly talk about that scourge of modern medicine, carcinoma of the pancreas.

It must be recognized that the therapy programs described here are by no means the extent of our program, and we have made major advances in nuclear medicine, positron emission tomography, and more recently with NMR; and one of the more significant

recent contributions is a new method for the diagnosis of that disease which occurs in elderly people, called Alzheimer's disease, that degenerative senility which occurs in elderly people. The slide will show you the diagnostic method which is used for that disease, where we give a labeled product which you'll hear more about today, fluorodeoxyglucose, a sugar, and in the normal brain that is distributed as shown on the left and on the right. In a person with Alzheimer's disease, you see the areas that look like they're at the back of the head, which are the degenerative changes which are found in Alzheimer's disease.

Lights, please, and that's all for this slide.

Now, what does the future hold, and where are we right now? The advances I have just described have been made in the face of sharply reduced budgets, and only since fiscal year 1982 the funding for nuclear medicine and therapy from DOE is down well over 20 percent. No significant new initiatives have been possible in the face of these funding constraints except through our own personal aggressive pursuit of alternate funding sources, such as the NIH. The staff of OHER in the Department of Energy has, however, been supportive of us in our search for these funds elsewhere, but have been unable to provide fiscal resources on their own.

The immediate need in our program is to identify a way to construct a replacement accelerator for the 30-year-old machines at Berkeley. This dedicated medical accelerator needs to be constructed in a medical environment. NIH has already provided us with $4 million for machine design, a task soon to be completed. The construction of such a machine is certainly consistent with DOE's mission and tradition, but the present budget outlook is such that we will have to approach the National Institutes of Health as the only reasonable alternative.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Alpen follows:]

Mr. Chairman, members of the subcommittee, I am Edward L. Alpen, Director of the Donner Laboratory, the biomedical research division of the Lawrence Berkeley Laboratory. I am also a faculty member of the University of California.

The Lawrence Berkeley Laboratory is a significant component of the Department of Energy's basic sciences research program. The Biology and Medicine program deals particularly with the application of techniques and scientific knowledge from the physical sciences to expand our knowledge of biology and medicine. The Donner Laboratory was founded in the 40's by Dr. John H. Lawrence, who was the recipient this year of DOE's Fermi medal for his pioneering efforts with his brother Ernest O. Lawrence, on development of applications of radiation technology in medicine. It is fair to say that the entire specialty of nuclear medicine had its birth at the Donner Laboratory. It has always been our great strength to have available to us the unusually competent physical scientists of LBL and the Berkeley campus as well as the advanced accelerator machinery developed by them. We have used this great strength to develop research and treatment applications of physical science to radiation medicine in general. Today I would especially like to describe the applications of a unique form of radiation, high energy accelerated charged particles, for the treatment of certain types of human disease that are very difficult or impossible to treat by other means. Finally, I would like to describe the applications, in our laboratory, of two advanced diagnostic tools, positron emission tomography and nuclear magnetic resonance imaging, in supporting the clinical research and treatment program.

While many cancers can be successfully treated with surgery, chemotherapy, conventional radiotherapy and various combinations of these modalities, many types of cancer have not been successfully controlled in the USA or elsewhere. For example, among those cancers treated by radiotherapy, even though the disease has not spread and is still confined to its organ of origination, as many as a third or more of those tumors treated are not controlled. These "failures of local control" account for about 100,000 deaths annually in the United States. It has been known for some time that improved local control of cancer might be achieved if a higher radiation dose could be given to the tumor while simultaneously sparing the adjacent normal tissue. A considerable advantage could also be gained if the radiation which is used could more effectively kill oxygen starved tumor cells which are resistant to X-rays employed in conventional radiotherapy. It is thought that the resistance to local control with conventional radiotherapy in the case of some tumors is the result of limited effectiveness of conventional radiotherapy in killing these oxygen starved cells.

In principle then, significant improvement in the local control of cancer could be achieved by two means: first, the more precise delivery of dose to the diseased tissue, a procedure which has come to be called "dose localization"; and, secondly, enhanced killing effectiveness for oxygen starved cancer cells. The second of these procedures forms the basis for the present national program evaluating the effectiveness of fast neutron beams for cancer control. There is already significant evidence that these biologically more effective neutron beams are giving better tumor control in some classes of cancer. The neutron beams, however, must by their nature sacrifice precise dose localization.

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As long ago as 1950 Robert Wilson, a physicist who later went on to become the first director of the Enrico Fermi National Accelerator Laboratory pointed out to his medical colleagues at Berkeley that accelerated charged particles had special properties that might make them useful in the treatment of deep-seated cancers. This special property of charged particles, known as the "Bragg ionization peak", is that the particles give up their energy more rapidly as they slow down, and most rapidly just before they stop. In other words, the track through normal tissue is less heavily irradiated and most of the energy is deposited in the tissue desired as a target. X-rays on the other hand, deliver their energy most intensely on just entering the body, and at greater and greater depth less energy remains for the tumor. Of course, with X-rays some fraction of the dose is also deposited beyond the tumor, the so-called exit dose. With charged particles this exit dose is minimal to non-existent.

Professor John Lawrence immediately took up this observation of Dr. Wilson's, and started to treat pituitary disease. Close to 800 patients were treated by Dr. Lawrence and his colleagues, with success rates well in excess of 90% for this very small organ located deep in the midline of the brain.

Accelerated charged particles, which we call "heavy ions" in our daily jargon, are the nuclei of atoms of any mass, stripped of their orbiting electrons. Because of their appreciable mass, these particles will only penetrate tissue if their energy or velocity is raised to very high levels in accelerators built for that purpose. Since the 50's we have used the 184" synchrocyclotron built by E.O. Lawrence in the 1940's and the Bevalac, built in the 50's and 60's, both of which machines can accelerate these ions.

This research on the biological applications of heavy ions has been supported at Berkeley by the Department of Energy and its predecessor agencies, the Energy Research and Development Administration and the Atomic Energy Commission under that portion of the Atomic Energy Act which directs that research be done towards applications of radiation and radio-isotopes in medicine and agriculture.

The research at LBL has already shown that Professor Wilson's predictions were indeed true, and furthermore that heavy-ions have many of the properties of neutrons for killing oxygen starved cells. The strong and comprehensive research program in the basic radiation biophysics of heavy ions at Berkeley laid a substantial foundation for our recent medical successes which I shall describe shortly. Before doing so however, I wish to make an additional point. The charged particle beams produced at the Bevalac are identical with the charged particle radiation field formed in space, and the evaluation of radiation hazards of charged particle beams in space can be evaluated at terrestrial locations only at the Bevalac. As with all radiation sources, their curative properties are balanced by their potential for danger. The longer manned missions of shuttle and possible space stations require careful analysis of this hazard which can only presently be evaluated at the Berkeley Bevalac or, with more difficulty and much more expensively, in space itself.

In 1974 the Office of Health and Environmental Research (in its predecessor form) agreed after a review by an expert panel to provide support for a further evaluation of the potential of heavy ions for the treatment of human disease. I can now report on some major successes for this program.

The Pituitary Program: As mentioned earlier, this pioneering effort by Dr. J.H. Lawrence clearly demonstrated the utility of helium ion beams for treatment of pituitary disease. This successful effort has now been closed at Berkeley since all research goals were achieved. The treatment is being provided as routine medical care at cyclotrons at Harvard; Uppsala, Sweden; and in Russia. We are under constant pressure to reopen this form of therapy, but since we have limited accelerator time, staff, and resources we are dedicated to moving into new research efforts.

Treatment of Melanoma in the Eye: There exists a fairly uncommon tumor in which a melanomatous tumor grows inside of the eye. There may be 1000 or so cases newly diagnosed each year in the U.S. The standard treatment has been the removal of the eye immediately upon detection of the tumor. We and the group at the Harvard/Mass. General Hospital cyclotron have been treating these eyes with very precisely localized radiation treatment with heavy ion beams. Our success rate is well over 90% for patients with over one year follow-up. We believe that even this can be improved with further research. Furthermore, vision is retained in the affected eye to some degree in all patients with disease control. For the larger fraction of these, visual retention is truly functional and useful. Between Berkeley and Harvard we can treat probably no more than a third of the newly diagnosed cases. Other therapies, such as the application of radioactive plaques to the outer surface of the eye, are being tested, but are as yet unproven.

Brain and Spinal Cord Tumors Requiring Precise Dose Localization: There is another group of cancers, generally in the central nervous system, for which heavy ion therapy has proved to be particularly effective. These tumors, of which there are several thousand newly diagnosed each year, are only rarely successfully treated by conventional radiotherapy or surgery because of the proximity of very sensitive neurological structures.

Our therapy group has now treated twenty or so of these patients with outstanding success considering that there is truly no alterative therapy. Of 17 patients for whom we have adequate follow-up, at least 14 are without present evidence of disease and can be considered to be treatment successes.

Arterio-Venous Malformations in the Brain: A very large number of people (approximately 10,000-20,000 new diagnoses a year) are found to have defects of congenital origin in the circulatory system in the brain. These defects are life threatening. Many can be treated surgically because their disease is in an accessible location. Many cannot be treated surgically because of inaccessibility of the lesion, perhaps as many as 2000-3000 patients per year. At Berkeley and at Harvard these patients are being treated with charged particle beams. In the Berkeley experience well over fifty patients have been treated and none treated have shown further bleeding. The follow-up must, of course, be much more extended, but we are very excited with these results. We are also deeply concerned that present facilities and staff at LBL and Harvard could treat no more than 3% to 5% of the newly diagnosed cases suitable for our type of therapy.

Of course, our touch has not been golden, and there are some diseases for which our success rate has been no better than for conventional therapy. I mention in particular carcinoma of the pancreas, a disease for which all modalities of therapy have proven particularly ineffective.

It must be recognized that the therapy programs described here are by no means the extent of the program at Berkeley. Major advances in nuclear medicine such as positron emission tomography, and more recently nuclear magnetic resonance tomography are making not only enormous contributions to diagnoses and evaluation of the patients described here, but have made important contributions in their own right as others in this hearing will describe.

Before looking to future development, let me reflect on the contributions made by the DOE program in the training of young physicians and scientists in the fields of nuclear medicine and radiation biophysics. We are, of course, part of a major university, and the laboratory has played a major role in the pre- and post-doctoral training of individuals in these specialties. Many of the leading physicians in nuclear medicine were trained at this laboratory. We continue to maintain a constant group of 30 or more PhD candidates in our training program, and usually have 5 or 6 post-doctoral trainees at any time. The funding for these programs has, however, generally shifted from DOE to NIH.

What does 'the future hold.' The advances I have just described have been made in the face of sharply reduced budgets. Since FY 1982 the funding for nuclear medicine and therapy from DOE is down 20% or more. No significant new initiatives have been possible in the face of these funding constraints except through the aggressive pursuit of alternate funding sources such as the NIH. The staff of the OHER has been supportive in our search for funds elsewhere, but have been unable to provide fiscal resources.

The immediate need is to identify a way to construct a replacement accelerator for the truly aged machines at Berkeley. This dedicated medical accelerator needs to be constructed in a medical environment. The NIH has provided $4M to design the machine, a task to be completed in the next few months. Though the construction of such a machine is consistent with DOE's mission and tradition, the present budget outlook is such that we will approach the National Institutes of Health as a reasonable alternative.

Let me thank the Members for their kindness in permitting us to appear here and describe briefly some of our successes as well as perhaps our frustrations.

Biographical Sketch - Edward L. Alpen

Graduated from the University of California, Berkeley in 1946 with a BS in Chemistry and in 1950 from University of California, Berkeley and San Francisco, with a PhD in Pharmaceutical Chemistry and Pharmacology. After a brief stay at George Washington University School of Medicine as an Assistant Professor of Pharmacolgy Dr. Alpen was recalled to active Naval service at the outbreak of the Korean war. He was ordered to the newly established Naval Radiological Defense Laboratory as a researcher on biological effects of ionizing radiation. Dr. Alpen remained at NRDL until 1965, during which time he rose to be the head of the Division of Biological and Medical Sciences. In 1965 he went to Pacific Northwest Laboratories of the DOE, operated by Battelle Memorial Institute, rising to the post of Laboratory Director. In 1975 Dr. Alpen came to the University of California, Berkeley as Professor of Biophysics and Director of the Donner Laboratory. His research interests have included hematological effects of ionizing radiation, radiation carcinogenesis and radiation effects in normal tissue.

Dr. Alpen is a councillor of the National Council for Radiation Protection and Measurements and a member of several National Scientific Societies. He received the Navy Science Medal in 1962 and the DOD Distinguished Civilian Service Award in 1963.

Mr. SCHEUER. Thank you very much. And now we'll hear from Dr. Phelps.

Dr. Phelps?

STATEMENT OF DR. MICHAEL E. PHELPS, JENNIFER JONES SIMON PROFESSOR AND CHIEF OF BIOPHYSICS, UCLA SCHOOL OF MEDICINE, LOS ANGELES, CA

Dr. PHELPS. I guess I would like, first of all to broaden the perspective beyond cancer, and I'd like to do that by considering some fundamental issues. I think these can be best addressed by considering issues in regard to the diagnosis—in fact, the origin—of all diseases.

It's important, I think, to remember, and you'll see a theme of chemistry throughout my discussion, that all the functions of the body are in fact chemical in their nature; all diseases are chemical in their origin, and there are no exceptions to that. In fact, all treatments are directed at altering the changes of disease at the chemical level, and that ranges from surgery that attempts to resupply nutrients to blood, to tissue; to resect tissue altered by chemical processes; to drugs which are just chemicals directed at chemical reactions of the body; to, in fact, even diet that changes the nutrients applied to the body, that is, chemicals. And even behavioral symptoms are an expression or a result of chemical changes in the body.

Now I'd like to, within that, resolve—deal with the issue of how one approaches human disease from a chemical point of view. The primary accesses that we have are through the body fluids—through the blood, through the urine, through the cerebral spinal fluid. However, those are fluids that drain the major portion, if not all, of the body, so they are very nonspecific to local diseases in specific organs.

The need is really to develop any technology that can approach locally the biochemistry or the body chemistry. I'd like to illustrate a technique that holds the greatest promise to do that and illustrate some of the examples that have been derived from it. The technique is referred to as positron emission tomography; it is an instrument-based technology that derived from the use of radioactive traces, radioactive elements that are substituted in the chemicals.

Now, the first thing that is realized is that there is probably no other single method in all of science that has taught us more about the body chemistry, about the living world, than what is called the tracer method, the use of radioactive elements and compounds.

Positron emission tomography is really a technology that extends that to the human being, that one can enter into the body in a safe and uninvasive manner and actually watch and measure the chemistry as it takes place. The best illustrations of that are the approaches in the use of label compounds, sugars, amino acids, fatty acids, the natural chemicals of your body in which we have substituted radioactive forms of the natural elements of carbon, nitrogen, and oxygen; and that is unique to this technology.

The studies that probably illustrate the capability of this best can be shown—two studies in epilepsy. The most common form of

epilepsy is called partial epilepsy; and when patients are not responsive to drugs they become candidates for surgery. In no technology to date is shown more accuracy in localizing eleptogenic focus than positron tomography. In fact, it has forced a clinical service to be run with this research technique for 7 years at UCLA. It has also shown and identified the biochemical deficits in childhood epilepsies that have never been seen before. It is being used to evaluate drug interventions to halt or change the course of seizure disorders.

A good example of early diagnosis is illustrated in a degenerative disorder called Huntington's disease in which the biochemical defect has been seen in 100 percent of the patients studied with this disease. Probably more importantly, since it is a dominant genetic disease, we know that 50 percent of the children actually carry the abnormal gene, so we have studied them in a state where they are presymptomatic, asymptomatic; that is, they have no symptoms of the disease. In fact, we have identified the biochemical defect of that disease in 50 percent of them; that is, at an early stage, even prior to changes that are reflected in altered behavior symptoms.

In mental health—mental health is a problem that has escaped every imaging technology that we have; in fact, it has confused and confounded almost every approach to studying either the symptoms or, in fact, the origin of the disease.

Studies have been performed to look at the biochemical changes in the brain and for the first time they have been identified in schizophrenics and in the affective disorders; depression/mania; and not only have they been seen when they are modified by either spontaneous recovery or drugs. In fact, the biochemical change can be measured and shown to return to normal, or exaggerated when the behavior is worsened.

In drugs, the problem in drugs ranges from issues around illegal drugs, or medical drugs. Illegal drugs in this country, such as the fact that an estimated 22 million Americans use cocaine, a similar number are involved with amphetamines, and the impact of that goes way beyond the $30 billion to $50 billion a year that are brought to the support of the illegal drug traffic. Obviously the social and economic problems of this country are based in large part by issues around drugs. The medical drug industry—I really don't even know the number, but it must be hundreds of billions of dollars. There are many problems that have to be examined in regard to drugs. The behavior modification drugs are a major part of our society, and there is no technology today that can study the issue of drugs in humans, the biochemical issue, other than positron tomography.

In stroke and cardiovascular disease, stroke is the largest monetary problem in this country in diseases. Not as many people die of it as cardiovascular or cancer, but the long-term debilitating features cause a large economic burden. The critical issue in stroke is to identify whether tissue is viable or reversible, so that it can be accessed by revascularization. That's true in both the brain and in the heart. So it is that positron tomography has shown the earliest identification of the ischemic event in both the brain and the heart

and, in fact, has shown the prediction of whether it should be bypassed or not.

Cardiovascular disease is a disease in which the first symptom in 50 percent of the people is sudden death, a very difficult symptom to deal with. Of the survivors of that, 50 percent of them will go on to sudden death, so there is a need to be able to deal with cardiovascular disease at even the asymptomatic levels as I illustrated with Huntington's disease.

We have shown the detection of marvelous changes in both adult and pediatric cardiovascular disease with positron tomography at the biochemical level. Now, all this comes to some concluding points with regard to the program in DOE.

Why is the program even in DOE? These technologies are nuclear technologies and they occur by internal technology transfers; most of the technologies were, in fact, developed for high energy physics, nuclear physics, radiation effects, and a variety of different areas of nuclear medicine. And these technologies are transferred and brought to focus in biomedical research and all the way to the point of clinical medicine. At a time when our laboratory has brought together the most distinguished faculty in the world, has been recognized with international and national awards, we find that the OMB has rewarded us by setting our 1985 budget to zero. We find this rather confounding if, in fact, not rather embarrassing.

Now, I'd like to conclude with two slides, and they will be very short.

These are additional studies of glucose metabolism in the normal human brain. Since glucose provides almost 100 percent of the energy, these tend to illustrate the rate of energy utilization. This is the most active area—it shows the area of the brain, that is involved actively in the process, going down the yellow and into the blue.

And these are—looking at the brain—they are normal when they've been given the tests.

We look at a cross-sectional scene, we see an activation of visual circuits. Inactivation of the auditory portion. We think about a simple mathematical problem, we think about the solution to the problem and activation of the cortex, that portion of the brain in the human being that differentiates him from all other animals, more than any other area of the body. The task of memory recall is activated in small, little structures. The simple tasks of work, such as moving and touching the thumb to the fingers, activates a part of the cortex called the motor strip.

We are using our own technology to study this for you, and we hope that you will see the points that we are trying to make. The hearing activates these areas of the brain; hopefully during the study, we hope that we will all think about the problems that we have and develop solutions for them and we hope also that we will remember the importance of the few months that we've all been at this work, and that we offer a lot of worth.

Now, the last slide—this is a CAT scan, an x-ray scan that shows the features that we've just revealed in diagnostic medicine, and that is the anatomical structure of the brain or the body; and this

study was, in fact, performed on a patient. This man was sent to the diagnostic clinic.

Here you see the biochemical studies, which are obviously not known. Anybody tell me which was taken of the head? He's been dead for 9 months.

Now, that shows the structure and anatomy that is necessary, but it is not sufficient for function. Anatomically, this patient is doing fine; biochemically, he is dead. [General laughter.]

May I have the lights, please?

Mr. SCHEUER. Have you finished with your testimony?

Dr. PHELPS. Yes, sir.

[The prepared statement of Dr. Phelps follows:]

TOPIC: HEALTH AND ENVIRONMENTAL RESEARCH
PROGRAMS OF THE DEPARTMENT OF ENERGY

Mr. Chairman, Members of the Committee, I appreciate this opportunity to provide information concerning the description and significance of the Department of Energy commitment to biomedical research. The enclosed statement is presented as representative of the nuclear medicine, brain, cardiovascular and cancer research communities involved in the use of radioisotopes for the study, diagnosis and treatment of human disorders. In this regard I will focus on the following:

1. Definition, origin, purpose and funding
2. Future
3. Positron emission tomography (PET) as a model of the field
4. Significance
5. Support

I. Definition, Origin, Purpose and Funding

I-1. Definition

The definition will be a broad description of "nuclear medicine", from basic research to clinical practice. In this sense nuclear medicine involves a large number of scientific disciplines and clinical practices that use radioisotopes for biomedical research, diagnosis and treatment. It reaches across fields in basic biomedical science such as anatomy, physiology, biochemistry, pharmacology, neurochemistry, micro/molecular biology, biophysics, bioengineering, biomathematics, and clinical sciences such as neurology, mental health, cardiology, oncology, medicine, and gerontology as well as others. The common thread that ties these fields together is the use of

biologically active compounds that are labeled with radioisotopes to study the biochemical basis of normal and disease processes of the body.

Nuclear medicine is unique in medicine in that it attracts professionals from all of the above disciplines. No other field of medicine has such diverse human resources. A major reason for this is that nuclear medicine develops methods and technologies for study and diagnosis which can be applied in all areas of medicine and biomedical research.

It is unlikely that any other single methodology has contributed more knowledge in the biological sciences than the application of compounds labeled with radioisotopes to trace and measure the functional, anatomical and biochemical basis of the living world. This approach called the tracer method, was developed originally by Von Hevesy for which he won the Nobel prize in chemistry in 1943. The significance of this method can be appreciated now, following the evolution of the method and the enormous number of discoveries that can be attributed to it.

I-2. Origin

Nuclear medicine as with many fields, has many origins. However, one of the most significant is the Congressional Atomic Energy Act of 1946 which stipulated criteria for the peaceful use of radioactive material for health and medical purposes. This Act spawned an era of research using radioactive tracers which led to the development of the medical practice of nuclear medicine in the 1950s. The success of this medical specialty has been described in numerous documents submitted to this Committee from the Society of Nuclear Medicine (about 10,000 members) and the American College of Nuclear Physicians (about 1200 members) and is demonstrated by the fact that today about 70

million nuclear medicine procedures are performed each year in U.S. hospitals and outpatient facilities (appendix).

This accomplishment and the significance of the studies (appendix) is quite impressive considering that nuclear medicine is only about 25 years old, a young age for medical practices.

I-3. Purpose

It is the underlying purpose of nuclear medicine to understand, diagnose and aid in the development of treatments of human disease by the use of biologically active compounds labeled with radioactive elements. The importance of the methods of nuclear medicine can be appreciated, when one considers the basic causes and cures of human disease. Consider the following facts.

a. There is a chemical (biochemical) basis to all functions performed by the body.

b) All human diseases have biochemical origins. Thus, if we are to understand them fundamentally and develop ways to reverse, slow progression and lessen patient suffering, the greatest impact will result from knowledge of the chemical signatures and character of disease.

c) The earliest stages of disease (i.e., when their principal cause is most evident and they are most responsive to treatment) can be identified by biochemical malfunctions.

d) All treatments of disease are directed at supplementing, blocking or destroying alterations in biochemical pathways. This is true in i) surgical restoration of blood supply of nutrients (i.e., chemicals)

to tissue or removal of tissue containing deranged biochemical processes of disease ii) drugs, which are chemicals with action directed at the biochemical nature of disease, iii) diet (i.e., nutrients or chemicals taken into the body), and even iv) modification of behavioral components of symptoms and stress which result from and/or produce changes in the body chemistry.

For all these reasons, and others, one must place importance and great value on any approach that unlocks the chemical secrets of disease and provides better insights for patient management decisions. Decisions are presently based largely on information that requires a great deal of inferences and deductions from indirect techniques, rather than direct measurements of the biochemical process causing the disease.

This concept, independent of any particular approach for accessing the required chemical information stands on its own merit. More challenging is the issue of how to achieve this goal. In the laboratory with animal, isolated tissue and biochemical research we have many excellent tools. The number of these tools and the knowledge derived from their use is increasing at a phenomenal rate especially in the last decade or so. New approaches are rapidly being developed and used in fields such as physiology, biochemistry, pharmacology, micro/molecular biology, genetic engineering, neurochemistry and cardiac metabolism. These advances have a common bond in the chemical nature of the investigations. Even anatomy, the study of the structure of the body, is developing and/or using techniques today such as immunocytochemical, neurochemical and monoclonal (i.e., chemical) approaches in which structures are characterized less by their cytoarchitectural description than by their specific chemical constituents and physiological functions.

With this movement and momentum in the basic sciences, how do we transfer this information to the patient setting or perform similar measurements in people? There are numerous ways in which the important and invaluable knowledge from animal studies can be used indirectly to develop an understanding of disease. However, two major practical problems limit our use of this knowledge. First, while basic science studies have been and will remain our major source of new knowledge at the fundamental level, animal models of disease are known to provide limited descriptions of human disease, which is our primary objective. Secondly we have limited access to chemical information in the living patient. Our principal access to biochemical information in the patient is body fluids (i.e., blood, urine, cerebral spinal fluid), which is of limited value largely because these fluids communicate with all or major portions of the whole body, diluting subtle changes from specific sites in individual organs. Tissue biopsies are limited by how often, where and when they can be taken, let alone the fact that conditions have changed once tissue is taken from the body. There are also a variety of empirical tests that provide rather nonspecific indications of chemical changes that are too numerous to mention.

Thus, the problem is to develop a bridge between the wealth of new knowledge and methods in the basic sciences and the clinical sciences that will allow us access to the local body chemistry. I will attempt to illustrate below a unique new approach to this dilemma which brings together <u>well developed</u> principles of biochemistry, chemicals labeled with radioisotopes, and tracer techniques with a <u>new</u> measurement device.

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d. Funding

Nuclear medicine, in the broader sense, not only had its origin in the predecessor of DOE, the AEC, but these federal agencies have been the mainstay of support and commitment. Almost all of the major technologies of this discipline have been developed through DOE (or by any other name) support. This support has led to the development of reactors and accelerators that produce the radioisotopes, discovery of different radioisotopes, radiation detector technologies, risk factors of radiation, imaging devices, radiochemistry, radiopharmaceuticals and many methods and applications developments. This is due to direct support to nuclear medicine programs and to numerous technology transfers within the greater DOE program of developments originating for other purposes (most of the developments listed above were in fact developed for reasons other than medicine). This transfer of knowledge and technology continues today.

Upon this base of support and commitment of DOE to nuclear medicine, additional financial support from universities, NIH, National Institute of Mental Health, state, commercial and private sector has been developed and expanded the resources and assets of the basic DOE program. The success of the program is not only scientific and clinical but also in terms of significance of the research investment dollar. The amount of taxable income (generated from about $10 billion/year in clinical services and about 400 million/year in commercial suppliers of instruments, radiopharmaceuticals etc) is quite significant. However, far more important are the past and present contributions to biomedical research and patient care along with the important potential of new developments that are occurring.

II Future

The most promising areas for the future in nuclear medicine are in the chemically based approaches in the area of i) techniques which employ the technology of computed tomography (CT), ii) labeled monoclonal antibodies for detection and treatment in many diseases such as cancer, and iii) development of new labeled radiopharmaceuticals and ways to produce them for more specific detection and measurement of the biochemical nature of human diseases. Rather than deal with generalities I will discuss a particular example, positron CT (commonly referred to as PET for Positron Emission Tomography).

III Example of PET

III-a Definition and Uniqueness

What is PET? It is a tomographic (i.e., to provide cross section images of the body) imaging instrument based on a mathematical/computerized technology.

What type of images are produced? Images of the chemical processes of the living/functioning human body (i.e., section I-3).

What is the origin of these chemical images and how are they produced? They are produced by replacing an element of body chemicals (i.e., sugars, amino acids, fatty acids, etc) with a small (trace) amount of a radioactive form of that same natural element (i.e., radioactive carbon-11 for nonradioactive carbon-12, radioactive nitrogen-13 for natural nitrogen, radioactive oxygen-15 for natural oxygen, radioactive fluorine-18 for hydrogen. This yields radioactive forms of the natural chemicals of the body, analogs of body

chemicals or drugs that are identical to the nonradioactive form. In animal research, radioactive carbon-14 and tritium are used to replace natural carbon and hydrogen in the same manner.

These labeled compounds are injected into a vein of a patient in such small mass amounts that they produce no alteration of the body processes. These body chemicals, both labeled and unlabeled forms, are delivered to organs of the body through the blood stream and there they participate in the chemical reactions of the body that underly its ability or inability to function properly. Thus these labeled compounds trace or follow the body chemistry.

These unique radioactive forms of the natural elements emit positrons, thus the name positron emission tomography, the radiation from which is detected external to the body and an elegant computer based technology in the tomographic instrument transforms this information into detailed cross sectional images (pictures) of the ongoing chemistry of the body. This allows one to watch and measure many specific biochemical processes in a safe and noninvasive manner.

What are the other ways to image the human body chemistry? To date there are none.

III-b Examples of Positron CT (or PET)

Normal Subjects: Studies have illustrated how PET can identify sites and measure the biochemial activity of the human brain as it performs sensory, motor and cognitive tasks in ways never before possible in the human. It has provided direct evidence that the human brain's response is not only dependent upon the type and content of input (music, language, etc) but also the

person's past experience and strategy used to analyze the input. Such studies are demonstrating how PET can provide a better understanding of how the brain works. The overwhelming majority of our knowledge about the brain is derived from animals (mainly rats). About 25% of the human brain, the frontal cortex, is unique to humans and is the part of the body that separates us from other animals more than any other aspect of the body. It is believed to be the primary or necessary site for the uniquely human functions of planning, logic, creativity, and many of our higher order cognitive abilities. It is also a primary site in mental health and behavioral disorders.

Epilepsy

Human epilepsy is a disorder in which patients typically have no gross structural abnormalities of the brain. Thus, standard radiological procedures which demonstrate anatomy, such as angiography, pneumoencephalography and x-ray computed tomography are typically normal in patients with this disorder. Functional studies of such patients with EEG has been the standard for diagnosis, characterization and management. In patients with partial seizures (most common human epilepsy), PET has identified for the first time in the living human the local biochemical deficit responsible for the EEG detected seizure activity. The accuracy is higher than any other technique with the exception of electrodes surgically implanted directly into the brain, where the accuracy is similar. The latter technique of course is not without trauma and risk. In patients with intractible seizures the localizing accuracy of PET is unrivaled, while EEG still remains a requirement to show that the area is eleptogenic. Localization however is critical for surgical resection of the tissue. At UCLA surgical success (total or partial removal of seizure

activity) occurs in greater than 98% of the patients. The value of PET in this procedure is such that a clinical service has been performed at UCLA since 1977. All subjects who are candidates for surgery are now required to receive a PET study, and because of the addition of PET about 1/3 of all patients will now bypass the depth electrode implants and go directly to surgery. With increasing confidence in PET, this number is slowly growing. In addition many patients whose EEG and behavioral indications were ambiguous before and were eliminated as candidates for surgical therapy are now receiving successful surgical interventions because of PET.

Childhood epilepsies (including petit mal, Lennox-Gastaut syndrome, infantile spasm and neonatal seizure) and generalized seizure in adults are now under investigation with PET which is illustrating the sites and distributions of biochemical abnormalities in these patients that are not evident by any other modality. In addition, research is being carried out to investigate the specific biochemical mechanisms that are deranged in epilepsy and to evaluate drug interventions for their confinement.

Hereditary Diseases

Although numerous hereditary diseases are being studied with PET, the results of Huntington's will illustrate the unique value of this technique. Huntington's disease is a dominantly inherited disorder with typical onset at the age of 30-50. It is clinically manifested by the triad of dementia, chorea, (a particular type of abnormal movement) and psychiatric disturbances. In patients with symptoms of this disorder, PET has shown 100% detection of the biochemical deficit in the central areas of the brain referred to as the basal ganglia. These changes are noted before any other imaging

modality such as the x-ray CAT scan and proton NMR, both of which primarily show anatomical changes that occur at later stages in the disease.

Since this is a dominant genetic disorder 50% of the children of patients with Huntington's disease will carry the abnormal gene. This serves as a good model system to illustrate another unique potential of any biochemical imaging technique. PET studies carried out at a time when there are no symptoms in children of parents with HD have demonstrated the genetic prediction in that 50% of them have shown a biochemical abnormality. This illustrates the sensitivity of this technique to identify chemical changes of disease in early states, even before they have reached a stage where detectible symptoms can be recognized. Studies are now being carried out using PET as a biochemical assay technique to measure the direct chemical response in the brain of HD patients to drug interventions. In addition, the findings with PET are being brought together with genetic linkage studies of this hereditary disorder.

Cancer:

Studies in brain tumors with PET can illustrate the value of this approach in cancer. The primary findings have shown that in vivo studies with PET appear to be as accurate as the pathologist in examining surgically resected tissue for the determination of the tumor grade (i.e., degree of malignancy). As is the case in other cerebral disorders, lesions have been detected before any other diagnostic modality. Studies have also shown the feasibilty of determining the actual cell turnover rates (i.e., growth rates) by measurements of protein synthesis (the building blocks of cells and membranes). The critical information (blood flow, membrane integrity and oxygen utilization) in selecting and evaluating therapeutic interventions has been

demonstrated and can only be provided at this time by PET.

Stroke

Although more people die of cardiovascular disease and cancer in this country than stroke, stroke is the largest single financial burden due to the long term debilitating nature of the disease. The limited amount of information and understanding of human stroke during the past decade has slowed progress in dealing with this disorder. Recently, studies have been performed with PET to demonstrate a critical issue, whether tissue is alive or dead after the stroke. This is the type of information that has been missing in the past to determine whether surgical revascularization is viable or not. Recovery is only possible if surgical supply of blood is returned to tissue that is alive, although injured, and has survived the stroke. These biochemical studies are providing the basis for improved patient management (conservative to more aggressive interventions) in a number of hospitals in this country, Europe and Japan. It is also being used to examine the biochemical and neuroanatomical distribution in the brain in regards to the biochemical mechanisms involved in recovery after stroke and potential ways to improve recovery.

Senile Dementia:

The most prominant forms of senile dementia are of the Alzheimer's type, multiple infarct dementia and pseudodementia or chronic depression. Senile dementia and effects of age are becoming an ever increasing issue in our population due to expanded life expectancy over the last 60 years and reduced

birth rate. The most important findings to date have been the identification and distribution of sites in the brain involved in these dementias. Although some of this was known from autopsy studies, these are performed at a stage that can be of little benefit to the patient. Biochemical studies with PET have illustrated the capability to differentiate these three disorders which have been very difficult to separate by standard conventional diagnostic criteria. This is important because their treatment and outcome are quite different. Studies are underway to use PET as an analytical tool to further identify the earliest changes in senile dementia, both the anatomical site and biochemical nature, and to evaluate drug interventions to alter the detected biochemical abnormalities.

Mental Health, Behavioral Disorders and Drugs:

The major mental health and behavioral disorders such as the affective disorders (depression, depression/mania), schizophrenia and various psychopathic behavioral disorders have eluded detection by any medical imaging technologies. In fact, they have been resistant to almost all studies to determine their basic nature and to clearly detect and diagnose them. This area will probably be one of the most imposing challenges for PET. However, studies with PET are being carried out at a time of great advancement in our understanding of the neurochemical basis of behavior from studies in the basic sciences (primarily animal studies).

Studies with PET in schizophrenia have identified biochemical abnormalities when all other conventional imaging technologies have shown no abnormality in the brain. In patients with depression, PET has shown the first detection of focal abnormalities in the frontal cortex. In addition, when

patients return to normal behavior spontaneously or drug induced, the PET study also showed a return to normality in the biochemical activity of the brain. When patients did not improve the biochemical deficit remained and when they worsened in behavior the biochemical abnormality worsened. This illustrates the first studies correlating direct biochemical changes in the living human subject expressing behavior abnormalities, and the direct biochemical measurement of drug responses of the human brain. The latter studies, along with other examples shown above, also illustrate the unique capabilities of PET to investigate the effect of drugs on the human brain. This is a major issue in modern societies where both illegal and medical drugs have grown in incredible proportion from a social, economic and therapeutic perspective. For example, behavior modification drugs such as cocaine are used by approximately twenty million Americans, amphetamines are used by a similar number and increasing, Valium and various other similar medical drugs are used at a very high rate to deal with the high anxiety and pressures of our society.

The medical drug industry is of enormous economic proportion and there is a need to develop a better way to develop and design drug interventions, assess the impact of drugs and in fact, in many cases, to determine whether they even work. Obviously, medical drugs represent an important means of therapeutic intervention. Drugs are chemicals that are directed at restoring or destroying chemical imbalances of human disease. The major problem rests in the fact that we don't know the chemical basis of most human diseases and therefore drugs are developed from indirect studies in animals, indications of chemical abnormalities at the confusing end stage conditions of autopsy or by hit and miss approaches of large drug trials. There are now many drugs that are being labeled with positron emitting radioisotopes to be studied in humans

with PET. This is one of the areas for which there is no other competitive modality to provide this key information in the actual living human.

Cardiovascular Disease:

Studies with PET have been providing a wealth of new information about the metabolic and biochemical basis of human cardiovascular disease. As mentioned earlier, cardiovascular disease is the largest single killer of people in America. In 50% of these people their first symptom is sudden death. In those who survive approximately 50% will die of sudden death. Thus, it is a disorder that must be studied and diagnosed with a technique that is sensitive to the earliest changes that occur, even presymptomatic (as shown in Huntington's disease above) but indicated for study by certain risk factors, (hypertension, smoking, high blood cholesterol and fatty acid levels, etc).

However, even now the survivors of a heart attack face a decision regarding various therapies, from surgical bypass to drugs or more conservative approaches. We have various existing conventional technologies (EKG, nuclear medicine studies, angiography, ultrasound) that can diagnose the presence of developed heart disease quite well, although as mentioned before early detection is a necessity. Detection of mild cardiovascular disease has been demonstrated with PET. However, after the diagnosis comes a difficult therapeutic decision. For example, is the patient a candidate for bypass surgery or not. As discussed above in stroke the important issue is whether tissue is alive and has survived the initial attack. This is a biochemical or metabolic question and for which only positron tomography has shown capability to directly make the evaluation. Recently, studies have been carried out in patients pre and post bypass in which in all cases where it was indicated from

PET studies that the patient (and in fact each segment of the heart) that would not recover from bypass, did not. In patients where PET studies indicated that the tissue remained viable and would recover, the patients did recover with one exception due to a surgical complication. Research studies are also being carried out to understand the biochemical nature, temporal course and prognosis. PET studies in childhood cardiac disorders such as Duchennes's muscular dystrophy have shown that the biochemical defects are seen before any other conventional technique and provide promise for assessment of potential therapies.

III-c Significance

The significance can be simply stated that PET represents a potential fulfillment in the real world of the dilemma posed in I-c. It is a unique technique in its developing stages that holds potential for advancing our understanding of the biochemical basis of human diseases. It is on one hand an exquisite scientific instrument for performing local biochemical assays in the living human subject. In this regard, it could indirectly result in the development of new diagnostic procedures and, most importantly, new therapies. With further advancement and technical developments it could also be disseminated to allow a biochemical examination of individual patients.

V. Support

Nuclear medicine is different than most medical specialities in that it does not have a primary patient care responsibility. It provides a diagnostic service. The quality and advancement of this service and the research base

provided by nuclear medicine techniques relies upon technology intensive developmental efforts. For example, NIH concentrates on the use of various technologies and methods to investigate disease. This component of nuclear medicine research draws upon NIH support for this purpose. However, basic technology development is not a principal mission of NIH.

The particular technology development of nuclear medicine draws heavily upon the nuclear technologies developed throughout the greater DOE program for nuclear physics, nuclear/radiochemistry, high energy physics, radiation safety/hazards, basic detector and semiconductor material and electronics research, biology and others. These DOE internal technology transfers and adaptations have been a key to the success of the medical research component of DOE.

Another critical factor can be illustrated with the DOE program at UCLA as a model. At UCLA the Laboratory of Biomedical and Environmental Sciences is an on-site laboratory which provides a sense of long term commitment and stability for scientists from many different disciplines to bring their varied expertise to a common problem defined by the programmatic commitment of the lab. Thus these efforts are problem, not discipline, oriented. The members of the lab are from about 25 different disciplines. Thus success of this approach is illustrated by such examples as the Laboratory of Nuclear Medicine which is the recognized leader worldwide and whose faculty have won many distinguished national and international awards for their achievements. The major pioneering efforts in nuclear medicine have and continue to occur by members of this laboratory such as the development of the first imaging device in nuclear medicine, medical accelerators, positron and single photon computed tomography, lung scanning techniques and many research and clinical study methods. Similar examples could be given for the other programs in the UCLA

DOE lab and the other medical science labs supported by DOE.

There are two separate issues to be considered. One is the concept of an on-site lab. This is critical for without it the whole concept developed in this presentation is dismantled. The on-site lab represents the longterm commitment to recruit and maintain excellent faculty, provide commitments to the solution of the more difficult and more important problems that will have long term effects. Research is a high risk area of endeavor requiring far sighted people who have the imagination, patience and commitment to look beyond where we can see today both in those who do the research and those who support it. In this context research should be separated from the term development. The former was just described, the latter has more predictable outcomes and shorter term goals.

Thus without the on-site commitment of DOE our lab, and others, would lose their base and would be destroyed.

The second and necessary part is funding without which the first part becomes as they say, academic. In the past years funding has fallen significantly behind inflation. This has been made up by "soft" monies from NIH, NIMH and the private sector. However, there must be limits placed on this or it will erode the stability of the lab. It should also be emphasized that UCLA has also contributed greatly to the lab by providing space in the medical center, partial support of some of the faculty (the overwhelming salary support of faculty staff and program still however comes from DOE), access to the broad resources of the university, direct financial support and help in raising private sector monies for major capital equipment. This is usually done in a matching way with DOE. The most significant contribution is the spirit of cooperation and support provided by the Dean, Sherman Mellinkoff, Associate Dean Frederick Rasmussin, Vice Chancellor Barber, Chancellor Young

and his staff. Our program is one of the most visible and productive programs in our university as a result of the quality of all involved.

There is clearly a need to maintain stable support which includes reasonable increases to account for inflationary and merit increases.

Since this is a technology intensive effort, capital equipment budgets are critical. This component of the DOE budget should be increased by 30 to 40%. Capital equipment as a principal resource has fallen behind and needs to be rebuilt.

We are willing and able to recruit matching money to support our program but without a long term security of our base DOE support the whole concept of this laboratory is broken.

Mr. SCHEUER. All right. Thank you.

Mrs. SCHNEIDER. Mr. Chairman, could I just ask a quick question?

Mr. SCHEUER. Yes, please do.

Mrs. SCHNEIDER. The slides that you showed us, Dr. Alpen, of the Alzheimer's disease victims, were those slides of patients that were dead or alive?

Dr. ALPEN. Those were functional studies of living patients in our laboratory, yes.

Mrs. SCHNEIDER. Just out of curiosity—I happened to serve on the Select Committee on Aging, and we had testimony before that committee where we had a medical witness come in and say it was really difficult to diagnose Alzheimer's disease, and there was no uniform method of diagnosis nationwide. And the conclusion was that the only way that you could be certain of whether a patient had Alzheimer's disease was after the person was dead, through doing an autopsy.

Dr. ALPEN. You can't even be certain then. I must say, though, that when that testimony was given to you it was entirely correct. The slide which I showed you is work which is less than 3 months old. It's been so exciting to the Alzheimer's community because they now have an in vivo diagnostic method which does, 100 percent of the time, diagnose the disease differentially.

Mrs. SCHNEIDER. Well, that's great. Now, the only place that——

Dr. PHELPS. May I answer that?

Mrs. SCHNEIDER. All right.

Dr. PHELPS. The confusion is in differentiating Alzheimer's from what's called multiinfarc dementia, or pseudodementia, the chronic depression, as Dr. Alpen discussed. In fact, three studies with positron tomography, the differential diagnosis is in fact fairly straightforward. Now, it needs to go to very early states, but they have clear and very distinct patterns that differentiate the disorders. Now, it is true that autopsy is typically the end-point description of

Alzheimer's, but it occurs at a time that it is of very little benefit or help to the patient.

Mrs. SCHNEIDER. Obviously. Well, is the Lawrence Berkeley Laboratory the only place where one can now diagnose Alzheimer's disease in a living patient?

Dr. ALPEN. By no means. By no means. There are probably a dozen places in the United States that have positron emission tomography equipment——

Mrs. SCHNEIDER. Excuse me. You are speaking to nonmedical professionals here. The positron——

Dr. ALPEN. The so-called PET, or PET scanner, as it's called in the vernacular, positron emission tomography. That's what Professor Phelps was just describing. And we are doing the same thing at Berkeley, and there are a dozen other places in the United States where they can do that, now that the method has been developed.

Mrs. SCHNEIDER. Where on the east coast?

Dr. ALPEN. Washington University, Harvard; that's all that comes to mind at the moment.

Mrs. SCHNEIDER. OK, that's fine.

Dr. ALPEN. There must be many others.

Mrs. SCHNEIDER. So there's Harvard in New England——

Dr. ALPEN. Brookhaven National Laboratory, certainly.

Dr. PHELPS. Cornell.

Dr. ALPEN. Cornell.

Mrs. SCHNEIDER. Cornell.

Dr. PHELPS. You see, we're from the West; we think of the Midwest as the east coast.

Mrs. SCHNEIDER. All right. Thank you.

Thank you, Mr. Chairman.

Mr. SCHEUER. Dr. Alpen, the Department of Energy remains the principal agency that is funding and managing research on various applications in medicine and biology. Do you think they're the best suited to carry on this research, or should it be perhaps transferred to another agency?

Dr. ALPEN. That's a difficult question which has been asked before. I believe the Department of Energy has, in all of its present and former forms, done a very distinguished job in managing a complicated program in which high technology is applied in medicine. It had that charge from the first days of the Atomic Energy Act, when the act gave the responsibility to the Department to work on radiation and agriculture medicine. It, today, is the only agency that is doing it. The obvious alternative for that is the National Institutes of Health. It would require, I think, major differences in the way the National Institutes of Health does business to deal with these very high technology medical fields that we work with. We certainly prefer working with the Department of Energy because it has been a useful functional relationship, but I have to say that if the funding continues as it is, it won't exist very long to work with.

Mr. SCHEUER. Dr. Phelps, the fiscal 85 budget figures show that the contract with your laboratory has been terminated. How do you feel this will affect progress in your area of research? How many people will be affected by it? Will your lab be able to survive the cutbacks?

Dr. PHELPS. Yes. I think there are two issues. There's one, the concept of a laboratory; and then two, the issue of funding. Of course, the second is necessary; otherwise discussion is, as they say, academic.

We have a DOE laboratory, onsite laboratory, and that is our base support. That is, it pays the major salaries and it is in fact the long-term commitment to our research goals. From that base we have gone out; we have gained access, very successfully, to NIH money, to the private sector component. In fact, we even to the commercial world. But all of that is based upon matching moneys from our base laboratory concept. If our DOE budget goes to zero, then so does our laboratory. The people will leave. We have recruited the best people in the world in our laboratory. You must have some base; you cannot build a house without a foundation.

Mrs. SCHNEIDER. Mr. Chairman, might I interject a question?

Mr. SCHEUER. By all means.

Mrs. SCHNEIDER. How many other laboratories are doing the same type of work that you are doing?

Dr. PHELPS. There are about 30 laboratories throughout the world.

Mrs. SCHNEIDER. And how about in the United States?

Dr. PHELPS. There are about 18 right now.

Mrs. SCHNEIDER. And how many of those are dependent on funding from DOE to do the same type of research you're doing?

Dr. PHELPS. Only a small portion of those, and it's an important point that was just mentioned, actually. The mission of the DOE Nuclear Medicine Program is the development of instrumentation and technologies and methodologies, and this represents a good example in which we have done that. NIH's mission is quite different than that. We are the laboratory that has contributed the most, in fact, to the development of positron emission tomography; and it has now been, in fact, disseminated to the major medical schools and institutions throughout the world.

Mr. SCHEUER. All right. It's been a very interesting panel. I'm going to ask unanimous consent for us to submit additional questions in writing to the panel.

Mrs. SCHNEIDER. I didn't realize you were going to dismiss this panel. I was just referring back to you, if you have any other questions. If you don't, I have about two more.

Mr. SCHEUER. Very good.

Mrs. SCHNEIDER. I——

Mr. SCHEUER. I would ask unanimous consent for us to hold the record open and submit additional questions in writing to the panel and give the panel another 10 or 12 days to get their answers in in writing, hopefully, at their earliest convenience. There being no objection, so ordered.

Mrs. SCHNEIDER. No objection.

I am curious to know if either of your labs are involved in the research into the disposal of the waste that is generated by nuclear medicine.

Dr. PHELPS. Research on how low level waste is disposed?

Mrs. SCHNEIDER. Yes.

Dr. ALPEN. No. We are not, at Lawrence Berkeley Laboratory, involved in that.

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Dr. PHELPS. No, we are not either, and that's actually another advantage of positron emission tomography in that they are all short-lived isotopes and they get rid of themselves. They have half-lives that last from about 2 to 20 minutes, typically, and so they decay; you don't have to deal with waste disposal.

Mrs. SCHNEIDER. Well, let me think what else I wanted to ask you a moment ago.

Insofar as the radioactive traces that I believe that you had mentioned, Dr. Alpen, you had mentioned that they were safe. Is this pretty much unanimous agreement by the medical profession, that it is a very safe technology?

Dr. ALPEN. The use of tracers, I think, Professor Phelps brought up.

Mrs. SCHNEIDER. Excuse me. I misnoted that.

Dr. PHELPS. Yes. In fact, the levels that we use are comparable to, if not in fact below, the acceptable Federal limits for all the diagnostic procedures using radiation. In fact, at the level of radiation that we use we, through billions of dollars and decades of research, have yet to measure the direct irreversible effect of radiation. We live in a world at risk of which radiation is, in fact—a part of our generation is growing up in the nuclear age—probably overrated in terms of the other risks, that is, the chemical and the atmosphere issues, let alone driving on the San Diego Freeway.

Mrs. SCHNEIDER. Not to mention the fact that anyone who is involved in dealing with any one of those risks will always point to the others as being equally, or if not more, influential in terms of risks. But, that point aside, Dr. Alpen, many of the programs that DOE has have been cut over the past couple of years and obviously it's had a series of negative impacts. Looking back over the past 5 years of DOE's fluctuations, how has that influenced the different programs that you are involved in?

Dr. ALPEN. Well, the principal influence is that we have to look to other means of support. In our own laboratory we've done that very aggressively, and the simple number is that if I look at the budget that I have in my laboratory from DOE 5 years ago, when it was 95 percent Department of Energy, today my budget is less than 30 percent Department of Energy; and I'm really, now, a multi-funded agency and I get my money, small bits at a time, from NIH. That means I can't take on expensive initiatives which require major investments, and I spend a very large amount of my time and my staff's time in getting money, small pieces at a time, from NIH, $50,000 packets.

Mrs. SCHNEIDER. And yet this administration is supportive of a policy that says that we shall pursue long-term, high risk research; but yet—pardon me?

Mr. SCHEUER. Have you got any evidence of that?

Mrs. SCHNEIDER. Well, the President has made that remark on a number of occasions, not only on this budget but also on the energy research and technology budgets. But yet we see a consistent reduction in all science research and development, and I'm just curious as to, you know, the fact that 5 years ago you were 90 percent dependent on the Federal Government; now you're only 30 percent dependent. I think that puts an argument in the hands of many conservatives who believe the Federal Government ought to get out

of research altogether. Can either of you, or would either of you, be interested in giving us an argument as to why the Federal Government needs to be involved in this research, if in fact you have gradually been successful in finding others to finance your research?

Dr. ALPEN. Well, of course, the other is still the Federal Government; it's the National Institutes of Health. And it's simply that they have a different style of doing research, which is small, individual grants, one person at a time.

Mrs. SCHNEIDER. I see.

Dr. ALPEN. And I would have to say that we find difficulty not only pursuing high risk research; we have difficulty pursuing low risk research. Our cancer treatments now are so successful that my principal concern at this point is to find time on the machines to continue research in the face of the load of patients that we are now getting for our very successful therapy. It's been demonstrably successful at this point.

Dr. PHELPS. I think, as Dr. Alpen pointed out, it is correct; it's a redistribution issue. You know, most of the major sources are Federal; but this administration has asked us to distribute our basis of support, that the State, the private sector, the commercial world must take a greater burden in sharing in the support of scientific investigation. In our laboratories, as Dr. Alpen mentioned, our labs have done that, but there is a point where you must put a limit on that because those are what we call soft moneys; they are periodic, and they will erode the base program. And if there is to be a long term commitment to the more serious issues, there must be a base.

I would also like to point out that in your previous question about the laboratories and positron tomography, if you trace, in fact, the origin of all the technology development transfer, it does go back to the Donner Labs at Berkeley, to UCLA, to Brookhaven, to Chicago, all of the DOE laboratories. And it is upon that base that the applications are disseminated.

Mrs. SCHNEIDER. Very fine. Thank you.

Thank you, Mr. Chairman.

Mr. SCHEUER. Before we wind up this panel, let me ask this. Can positron emission tomography help us understand why people become victims of certain scourges? Is there a certain previous position? Can we test them through tests to see if there is a certain predisposition, let us say, at the youth end of the scale to drug addiction? At the elderly end of the scale, to Alzheimer's disease? Can this be used in preventive medicine?

Dr. PHELPS. Well, I go back to the basic issues. The fundamental nature of that is the chemical question. I mean, that is the origin of the disorders. Every time you do something, when you talk to me, when you think, it is because there are neurochemical actions that take place in your brain. And the bulk of our knowledge originates in animals, and principally the rat, which we could use as an example for many things; but the problem that we're really interested in is how the human brain works, and the human brain is different than a rat. Twenty-five percent of your brain does not exist in the rat, and it is that portion of the brain that allows you to be so human, this portion up here [indicating]. And if we are ever to understand those issues in a human setting, we must bring

chemistry to the healing. That's what drugs are; they are chemicals. They modify the chemical actions of your brain. There are no opiates in the brain; there are endorfins and enkefolins [phonetically], chemicals that act like that. We understood that because people used opium and it changed their behavior. And we're in an era where there's a tremendous expansion; we're in the largest expansion in biomedical research known to mankind. And if you look at physiology, neurochemistry, molecular biology, genetic engineering, pharamacology, they have a common theme to them, and it is chemistry. Even the anatomists who look at the architecture of your body are turning away from that and going to the chemical composition and the functions it performs.

Mr. SCHEUER. Let me just interrupt you. Can you give me a simple answer to my question? Can PET be used to identify a predisposition on the part of a youth, let us say, to drug addiction? That's a behavioral condition that might come from the chemical condition in the brain. Or could PET be used to identify a predisposition on the part of a person approaching old age to Alzheimer's disease; and therefore, having identified that predisposition, either in the case of the youth and drug addiction, or in the case of an elderly person and Alzheimer's disease, could some kind of preventive medicine approach be adopted? And a chemical or therapy applied to remedy or counter that predisposition?

Dr. PHELPS. Mr. Chairman, you'll have to forgive me. I'm Irish, and my answers always tend to be a little long. Yes, I think there is no other alternative that offers this great a hope to, in fact, do that. I tried to illustrate, in fact, that we have studied behavioral disorders, depression/mania in fact a variety of drugs in which we have shown for the first time those chemical alterations in the brain, in a specific area of the brain, in the frontal cortex. That is, we can show for the first time that there is a chemical problem in the brain in the people that drop into these behavioral states. We can also show a change with the behavioral state. We can modify it with drugs. That's the first time that we have been able to do that. So it's very hard to say "absolutely, no question" but we have greater hope today than we've ever had before.

Mrs. SCHNEIDER. A few little questions. Where are we going on the costs of applicability—or not applicability, but access to this technology for the average citizen?

Dr. PHELPS. Well, that's become another part of our mission with a changing world. We have put forward the efforts to develop the technology and prove its viability and importance, and in fact to develop a new concept in medicine. But today we must be more cost-efficient and cost-aware. So in fact we, in our laboratories at UCLA and at Donner and the other DOE laboratories, must now turn to developing more cost-effective, smaller, more clever approaches to contain the cost in these technologies. And that's in fact what we are doing.

Mrs. SCHNEIDER. In your Alzheimer's research have you identified aluminum as being a potential part of——

Dr. ALPEN. No. We have identified nothing.

Mrs. SCHNEIDER. Are you familiar with the studies that are going on about aluminum?

Dr. ALPEN. Yes, ma'am, I am but there is, in our opinion at this point, really no strong basis for that argument. There might be a slow virus——

Mr. SCHEUER. There might be what?

Dr. ALPEN. A slow virus, one which grows very slowly——

Mr. SCHEUER. Slow virus?

Dr. ALPEN. A slow virus, yes, sir, one which grows very slowly. There's a disease in sheep, called scrapey, which has many characteristics of Alzheimer's disease. We have had this diagnostic procedure for only 3 or 4 months. It's going to be a very powerful tool now, and allowing us to look at the early stages. We cannot, to answer your question, Mr. Scheuer, we cannot do any predisposition studies at this point; but the future is still ahead of us. And we are developing new and cheaper methods. We're looking at single emission, single photon emission tomography as a means of providing this technology in the field cheaply and to more community hospitals than can afford the PET methodology.

Dr. PHELPS. Let me go back to an example I gave you of Huntington's Disease. This is a genetic—dominant genetic disorder; 50 percent of the children have a predisposition to having this disease, but you don't——

Mr. SCHEUER. Which is this?

Dr. PHELPS. Huntington's disease. But you don't know—all we know genetically is that there is a predictability, but no technique has ever been able to identify which of those people have the predisposition. No technology. That, in fact, has been clearly shown with positron tomography, is identifying that 50 percent of those, before they have any symptoms, any expression at all, that a biochemical abnormality does exist; and it remains within the compensatory capability of the brain to inhibit any symptoms.

Mr. SCHEUER. Well, the very fascinating quality of your testimony has produced a situation where we're way behind schedule. So we've enjoyed it and we've benefited from it, and we're very grateful to you for your enormously stimulating testimony, and we thank you.

We will now move on to the next panel. Dr. Victor Bond of the Brookhaven National Laboratory, Dr. Warren Sinclair of the National Council on Radiation Protection and Measurement, and Dr. Chester Richmond of the Oak Ridge National Laboratory.

All right. As I mentioned before, your prepared testimony, all of you, will be printed in full in the record. So perhaps you would chat with us informally, taking no more than 6 or 7 minutes, giving us the highlights of your testimony. Of course, anything that you've heard from the witness table today or anything that you've heard from Congresswoman Schneider or myself—and then, I'm sure, after the three of you have given us the benefit of your thinking, we'll surely have some questions.

First, let's go in the order in which they're listed here. Dr. Victor Bond.

STATEMENT OF DR. VICTOR P. BOND, SENIOR SCIENTIST AND ASSOCIATE LABORATORY DIRECTOR FOR THE BIOMEDICAL AND ENVIRONMENTAL SCIENCES, BROOKHAVEN NATIONAL LABORATORY, UPTON, NY

Dr. BOND. Thank you, Mr. Chairman. I am pleased to be here.

I shall speak to the questions asked of me in the letter from you, Congressman Scheuer, in the order asked. The first question was, what makes a cell cancerous after an insult from radiation? That's a difficult question, and a completely honest answer probably should be that we don't know, but I believe that that would be misleading. There is, in fact, a great deal of evidence, which I will summarize in very oversimplified and brief form, to suggest, at least for some cancer types, the critical subcellular lesion produced by radiation exposure may be a chromosome translocation in a stem cell. That is to say, part of one chromosome, an oncogene normally present on one chromosome and responsible for triggering cell division, may be relocated on another chromosome and is thus placed in a new gene environment. In its original or normal location the oncogene responds only through mechanisms involving external growth or self-proliferati of stimulating factors originating from the tissues. This appears to be a normal constituent feedback or self-proliferatio regulating mechanism.

However, in the translocated position of the oncogene, the oncogene is released from such restrictions and may cause cell division that is not under normal control. This could constitute malignant initiation of the stem cell.

I'd like to refer to a specific example of the results of such oncogene translation, but not specifically involving radiation, which has to do with a human cancer, Burkitt's lymphoma. The work I refer to is that of Carlo Croce, C-r-o-c-e. Burkitt's lymphoma can arise from so-called "b-lymphocytes", which have genes that are continuously active for antibody production. They also have an oncogene responsible for triggering division. However, the oncogene is out of place in that it is located on a different chromosome near a gene responsible for antibody production. The implication of this work is that if an oncogene responsible for triggering cell division is translated from its normal location to another choromosome where there is an active gene, in this case, with the B-cell, one that is continuously producing antibodies, then the cell division-triggering oncogene may also be switched on continuously; that is, what switches on a normal gene could also switch on the oncogene if it's located near that normal, active gene. So that is to say that the gene responsible for cell division is no longer under control, only of the normal external stimuli, and is able to divide, presumably continuously. This is a most significant development.

It is quite possible that this overall growth factor, receptor nucleus activation mechanism for switching on cell division, may fit a number of tumors. Since radiation definitely does cause chromosome translocations, this may be a principal mechanism through which radiation may induce cancer.

Now, this type of basic research is exciting and it's important and must be encouraged. However, a main purpose of research in carcinogenesis overall is to be able to predict, in human popula-

tions, the expected excess incidence of cancer after exposure to a low level of radiation, or other carcinogens. This kind of quantitative prediction requires knowledge about physical mechanisms leading to functions relating the amount of exposure to the expected excess cancers in the population.

This brings me to the second question asked by Congressman Scheuer, namely, whether the role played by promoters in carcinogenesis. It is generally agreed that cancer is a complex, multistep process and that without promoters, initiated cells may not be able to be expressed as cancers. Further, promoters can and do change the shape of exposure response curves, particularly with high level radiation exposure. Some work with promoters can be done in tissue culture in which dimmer light transformation can at least be accelerated by the addition of external promoter substances, for instance, such substances as phenobarbitol and DDT are promoters. However, some of these studies in culture, those done with cells that were partially transformed in becoming adapted to cell culture, to me, appear to be at odds—the results of these cells appear to be at odds with those in animals. Also, the endogenous promoters of animals, for instance hormones, may act quite differently than do foreign, external promoters; and the endogenous promoters are affected by high levels of radiation themselves. Therefore animal studies must be done in addition to subcellular and molecularbiological studies in order to obtain the necessary information for quantitative prediction in man.

There are a number of additional reasons given in my written testimony for animal studies, many involving promoters. I shall simply mention these, and say that they are discussed in the written testimony.

Synergisms are important to understand between radiations of different LET or between different radiations and chemicals. Promoters obviously play a role in the answer to that question. That latent period that is well known for human cancers obviously—or most likely—involves promoters. This has practical bearing in that one may have a period of years to do something between initiation and——

Mr. SCHEUER. Dr. Bond, I wonder whether you could begin to sum up, because you're beyond your seven minutes.

Dr. BOND. All right, fine. Then I would like to go to the last part. I was asked to comment on the impact of the 85 budget on our biological environmental research programs at Brookhaven. A detailed impact statement is provided in my written testimony. Suffice it to say here that our ability to do this kind of research has decreased because of increasingly stringent budgets over the past several years. The impact of the fiscal year 1985 budget is particularly devastating, and in effect it amounts to a reduction of about 25 percent in dollars and the loss of about 68 persons. This brings into question for the first time the continued viability of our DOE-supported biological and environmental research programs at Brookhaven.

Thank you, sir.

[The prepared statement of Dr. Bond follows:]

Testimony of

Victor P. Bond

Before the United States House of Representatives

Subcommittee on Natural Resources,

Agriculture Research and Environment

of the

Committee on Science and Technology

6 March 1984

Department of Energy Programs Involving Both Uses and Unwanted Effects of Ionizing Radiations

Victor P. Bond[1]

Introduction

The contributions of the Department of Energy (DOE) to research in radiation biology, environmental sciences and nuclear medicine, can be divided into two major categories: 1) investigative work addressing the long range problems of concern to the DOE, particularly those of small exposures of the population to radiations and other mutagens and carcinogens, and 2) investigative work in nuclear medicine, including diagnostic and therapeutic procedures. For work in both of these broad categories, the DOE provides and maintains unique and state-of-the-art facilities, to be used not only by scientists at the host Laboratory, but by an even larger number of university and industry scientists throughout the United States and abroad.

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[1] Senior Scientist and Associate Laboratory Director for the Biomedical and Environmental Sciences at the Brookhaven National Laboratory, which is operated for the Department of Energy by the Associated Universities, Inc. I have been engaged in research in radiation biology and nuclear medicine for over 30 years, the first 5 of which were spent with the Naval Radiological Defense Laboratory in San Francisco. At Brookhaven I was initially in charge of the Division of Microbiology in the Medical Department, then Chairman of the Medical Department, and currently Associate Laboratory Director. I also hold appointments as Professor of Medicine at the Health Sciences Center, State University of New York at Stony Brook, and Adjunct Professor of Radiology at Columbia University. My research work has been concerned with the kinetics of cell proliferation in health and disease, cellular and mammalian radiobioloby, nuclear medicine and experimental radiotherapy, and experimental mutagenesis and carcinogenesis.

My intent in this brief presentation is first to provide some examples, many from my own experience, to illustrate the progress that is being made, and the problems that remain with respect to achieving a satisfactory understanding of the effects of "low level" radiation exposure (i.e., low doses of radiation, or higher doses delivered at very low dose rates). Carcinogenesis, and particularly the importance of promoters and of animal research, are stressed. My view is that new knowledge is being accrued at a substantial rate, so that continued efforts on a number of related fronts can be increasingly productive. The questions asked in investigative work can now be much more sharply formulated, so that the experiments can be much more decisive.

Examples are then given of the uses of radiations and of radiotracers in the metabolic study, diagnosis and therapy of disease, including cancer and disorders of the brain. The situation parallels that stated above for radiobiology. That is to say, new ideas and the exquisite new machines that are now becoming available, give promise of advances in these areas at a rate that could be only vaguely perceived a decade ago.

The last section summarizes the impact of the FY 1985 budget on Brookhaven's biological and environmental research programs. Because of stringent budgets over the last several years, the FY 1985 budget is particularly devastating in that it begins to bring into question the viability of the program.

Radiation Effects, Long Range Approaches

Study of the biological effects of radiation, particularly mutagenesis and carcinogenesis, requires approaches through several disciplines, i.e., physics, biophysics, and molecular biology including structure and function. Also, the problems must be attacked at several levels of organizaion, i.e., subcellular, the single cell, the organ, and the complete organism, including animals and human beings. Clearly the complexity of biological organisms increases as one goes from "simple" systems such as viruses and bacteria, through eucaryotic cell systems, and into the realm of complex organisms such as the mammal. Also, it is well recognized that carcinogenesis is a multifaceted process that may involve a number of steps, including an initial induction or "transformation" of one or at most a very few cells, as well as "promoters" or other substances that determine if and when an induced cell may proliferate to become expressed as a neoplasm in the host organism.

Enormous strides have been made in the past few years in understanding factors at the molecular biology level that contribute to the carcinogenic process. It is obvious that research of this nature must continue at a healthy pace in order that carcinogenesis, whatever the physical or chemical agent involved may be, can be understood and perhaps the effects ameliorated. An excellent case for the importance of this kind of work was presented before this Committee, by Dr. Richard Setlow of the Brookhaven National Laboratory, one year ago. I should like to augment that testimony, by enlarging on requirements that must be met if we are to understand adequately the full extent of the carcinogenic process, and be able to predict quantitatively the

expected excess incidence in an exposed population. To put it simply, just as one is unlikely to gain much insight into subcellular biological mechanisms by use of biophysical principles or the study of animal or human populations alone, so one is most unlikely to learn how to characterize and then predict effects in these populations by limitation of studies to the subcellular domain. The situation is reminiscent of the older discussions on the relative merits of studies in general cell biology vs. those in animal and human physiology. Both kinds of studies must proceed in parallel.

To illustrate and perhaps to place an upper bound on the range of studies necessary, consider first those on human beings exposed to radiation. For instance, the follow up observations on those exposed in Hiroshima and Nagasaki represent a most important resource and a classic example. Collection of data on these populations is enormously productive in indicating that high doses delivered in a short space of time can induce more cancer than would otherwise appear in the population, and that even this extensive exposure to a large population does not cause an epidemic (i.e., the increase in overall cancer rates has been less than one percent). These studies also put crude bounds on the type of "dose-response" functions to be expected. However, even though the doses are currently being reevaluated, statistical limitations do, and undoubtedly will continue to preclude obtaining answers to some important questions, namely the shape of the overall exposure-response curves for different cancer types, the expected incidence at low doses, and the dependence of the severity of the population effect on the temporal distribution of dose.

Also, with respect to radiations of different quality or linear energy transfer (LET), a dose-response relationship for fast neutrons was derivable from the earlier dosimetry for Hiroshima. However, the dose reevaluation indicates a paucity of fast neutrons in Hiroshima, so that a dose-response relationship for neutrons can no longer be derived. Obviously, then, studies between the two extremes of molecular biology and human epidemiology, i.e., neoplastic transformation of cells in tissue culture and in animals, using radiations of different LET, are mandatory to complete the overall picture. Additional reasons for this position are now elaborated on.

Consider first exposure-response relationships in rather simple autonomous systems, more specifically chromosome abnormalities which are increasingly suspected of being associated with at least some carcinogenic processes. An example of the types of exposure-response relationships obtained is given in Fig. 1, for radiations covering a wide range of LET's (from work of Dr. Skaarsgard). Note that the initial segment of all of these curves is quite consistent with a "linear, no threshold" relationship. Also, the curves for high-LET radiation appear to be linear even to high dose levels; that for low-LET radiation, "linear-quadratic". The high-LET curves are linear over a wide range of exposure because of the virtual absence of complicating factors, such as concomitant cell lethality or hormonal influences.

However, now consider similar curves for carcinogenesis, such as those shown in Fig. 2 for radiation-induced tumors of the Harderian gland, in the eye of the mouse. Note first the lower curve, for fast (fission) neutrons alone. The initial part is consistent with linearity, as would be expected

from the curves in Fig. 1. However, the curve then bends sharply to the right. This change in shape from linearity was suspected to be due to a depletion of hormones normally present (i.e., "endogenous promoters"), caused by the higher doses of radiation. That this almost certainly is true is shown by the upper curve involving pituitary transplants ("isographs"), which when placed in the animal, restore the hormone balance. As a result, the initial curve continues to be consistent with linearity up to higher doses, as observed in the less complicated systems in Fig. 1.

The point of the above is that important complications such as that illustrated, in which the final curve is shown to be a composite of two curves reflecting different mechanisms, would not be appreciated in the absence of such animal studies. Also, there are potentially-important practical implications. For instance, it is now known from Hiroshima and Nagasaki that young girls exposed to relatively high doses of radiation do develop an appreciably higher incidence of breast cancers, but only much later in life when this type of cancer would normally appear. Also, it was shown long ago at Brookhaven that the full expression of radiation-induced breast tumors in female rats can be encouraged or nearly prevented by maintaining normal or reduced estrogen levels, respectively, after the induction (i.e., the estrogen is an "endogenous promotor"). It is entirely possible that, through a better understanding of "promoters" for breast tumors and other types of cancer, endogenous or exogenous, it may be possible to devise means of preventing the full expression of some tumors.

As a "simpler" system in which to study tumorigenesis, extensive investigations have been made of neoplastic transformation in vitro. These highly illuminating studies have brought out apparent differences between findings in these systems and those found in some animals,and in other in vivo systems, which demand further investigation. Much of the tissue culture work has been done with C3H/10 T 1/2 cells or similar systems, in which neoplastic transformation appears only if the cells are allowed to go to "confluence" (i.e., entire dish is covered with cells in contact, so that growth is stopped by contact inhibition phenomena). A few of the cells may then grow into colonies that resemble neoplasms. Highly quantitative results are possible; however certain critical differences having to do with linearity, and the temporal dependence of the slope of the initially linear curves have emerged. The question then arises, which results should be considered applicable to the human being? In particular, does confluence and thus perhaps contact inhibition simulate the in vivo condition in the human being? Although a great deal more work will be necessary to understand the reasons for the differences, obviously such understanding must be achieved.

Another area of substantial importance is that of "synergistic" effects, between radiations of different LET, between radiation and chemical carcinogens, and perhaps for interactions between cell induction and the "promotion" phases. "Synergism" in this situation means simply that, if cells of animals are exposed to two different carcinogens, the excess incidence in the exposed animal population is greater than that to be expected by simple addition of the contribution expected from each agent separately. That is to

say, the agents may reinforce one another to yield a larger incidence. Although relatively few clear cut examples of synergism have been found, those found appear to occur only with high exposures and exposure rates. Some still preliminary work at Brookhaven, with various combinations of radiations and chemical carcinogens, has shown a lack of synergism for the cell induction process at low doses, with synergism seen, if at all, only with large exposures and exposure rates.

The question of synergism as expressed above does have substantial practical relevance, for instance with respect to the "probability of causation" approach. This method has received substantial attention recently in connection with litigation involving individuals with a cancer, and an implication that a specific prior radiation exposure may have caused that cancer. Because cancers have no "markers" identifying the causative agent, the probability of causation approach has been introduced as a method to calculate the probability that the specified cancer was in fact caused by the specific dose. The range of situations to which the method may be applicable in its simplest form depends directly upon the question of synergism. This is because the ratio used is a probability only if a given agent, e.g., radiation, is known or believed to have been the sole or exclusive cause (as opposed to a "shared mode", in which two or more agents may have contributed causally to the same specified cancer).

More attention is needed to biophysical approaches to explain the initial "linear, no threshold" exposure-response relationships, that are well documented for both high and low-LET radiations in "simple" systems, and for high-LET radiation with at least some kinds of tumors in animals. The initial

linearity and a lack of a threshold can now be explained from rather simple considerations of the statistics of rare events, augmented by microdosimetric data that allow one to determine the number or proportion of cells struck in a "collision" with a charged particle, and the amount of energy deposited in critical volumes within each individual cell. In short, the "absorbed dose" to the organ becomes, at very low doses, the number of cells "dosed", and not the "dose" to the cells relevant for carcinogenesis. The significance of this is that, with low doses and "single cell" effects such as carcinogenesis and mutagenesis, the function that is currently being called a "dose-response" curve is in fact a quite different function with different variables. Therefore the interpretation of the "linear, no threshold" response becomes quite different from that usually perceived. Extensions of considerations of this nature might help to ameliorate the confusion and concern now rampant with respect to "low-level radiation exposure". It is this kind of modeling, which goes far beyond simply mathematical fitting of curves, that permits explanations in terms of biophysical mechanisms. It permits one to describe exposure-response relationships more accurately, with the promise of improved predictional capability.

It will be noted in the above example that high-LET, rather than low-LET radiation was emphasized. This illustrates the point that it is much easier to compare the responses of biological endpoints in different species, and of different biological endpoints in the same species, by use of high-LET radiations. This is because, the effect per unit exposure is greater, so that one can find effects at lower exposures and determine the shape of the

curve(s) more easily and accurately. For instance, one can have confidence, in studies with "simple systems" such as that shown in Fig. 1 in which adequate statistics can be obtained, that there is, with radiations of different LET, a "fanning-out" of proportional curves, including an initial linear curve for low-LET radiation. In animals, one can obtain relatively accurate curves for low doses, but only with high-LET radiations. It is not possible to determine the curve for low-LET radiation at low doses, because of statistical limitations. However, if one obtains a similar fanning of curves for animal carcinogenesis for high-LET radiation (as one appears to obtain--see Fig. 3 from Dr. R.J.M. Fry), but questionable or no excess effects at low doses for low-LET radiations, strong support is lent to the thesis that the absence of findings with low-LET radiation and with low doses, is due to statistical inadequacies and not the absence of an initial linear term.

Carcinogenesis with "internal emitters" also demands studies far beyond those on subcellular mechanisms of cell induction or transformation. That is to say, with internal emitters it is extremely difficult to identify the relevant cells with respect to carcinogenesis (often true also with external radiation), the distribution of isotopes among these cells, and how that distribution changes with time. Consequently the total dose and dose rate to the cells are frequently known only poorly. Therefore, with respect to describing or predicting what may happen in the intact animal, there is no recourse but to do the relevant studies on intact animals and, to the degree possible, on human beings.

In short summary of the above obviously-incomplete and sketchy presentation, an effort has been made to show that work must continue over a wide spectrum of carcinogenesis-related activities. That is to say, although it is difficult to over-emphasize the importance of continuing basic work at the subcellular and molecular biology level, it is also quite important to continue to do mechanistic studies at increasing levels of biological complexity, up through animals and man. Without studies over this broad spectrum it will not be possible to understand adequately the complete processes of carcinogenesis, to describe agent response relationships, or to predict population effects in man from exposure to such agents.

Radiation is often taken as the model for carcinogenesis in general, including chemical carcinogenesis. However, it is not at all certain that the initiating and following events are the same or similar for radiation and chemical carcinogenesis. It therefore remains to be seen, and must be determined, the degree to which the radiation model should be used across the board for carcinogens and mutagens other than radiation.

Although agencies other than DOE, in particular the NIH, have been able to provide support for radiation effects studies, by far the largest contributor has been the Office of Health and Environmental Research of the DOE. However, OHER support in terms of person years of effort has steadily declined, and the rate of decline appears to be becoming more marked. This is most unfortunate at this time when, with the current rate of increase in our knowledge of the subject, continuing research is fully expected to be even more productive.

The long-term effects of the reduced rate of support goes beyond simply a reduction in the rate of acquisition of new knowledge and understanding. For some time there has been an erosion in the number of individuals coming into the field in general, and particularly those interested in dealing with carcinogenesis in the broad and important areas between studies at the molecular biology level, and epidemological studies in the human being. Thus the capability for carrying out such studies is being lost, just at the time when the importance of studying "promoters", "synergistic effects", and other areas necessary to understanding of the full carcinogenic process are becoming increasisngly appreciated, and improved methods of study are becoming available. Also, special and costly-to-replace facilities designed for the study of these essential aspects of carcinogenesis will continue to be lost with dwindling support.

The Uses of Radiation in Diagnosis and Therapy

Although justice to the subject can be done only with an extensive treatise, only three examples of the uses of radiation in the therapy of cancer, and two in diagnosis will be given. These examples are drawn principally from experience at the Brookhaven National Laboratory, from work supported in part by the OHER and partly by the NIH. They illustrate the interplay of new concepts, knowledge, techniques and rather exotic machines, in bringing new diagnostic and therapeutic ideas and approaches to fruition. The examples illustrate the fact that a number of ideas cannot be pursued without the availability of appropriate equipment and machines, some highly sophisticated and expensive.

Physiological Targeting of Stable and Radioactive Isotopes to Tumor for Radiotherapy (R. G. Fairchild)

With conventional radiotherapy, it is difficult to achieve adequate dose to target tissues (tumor) while at the same time sparing non-target (normal) tissue. Therefore, it would clearly be desirable to target radioactive isotopes to tumor cells physiologically, in order to achieve dose localization at a cellular level, as well as to seek out remote extensions of growth. In practice, systemic application of radionuclides is often precluded by competing uptake in rapidly proliferating normal cell pools such as bone marrow and gut. This problem can be circumvented by targeting stable isotopes which later can be activated with appropriate external beams.

1. Neutron Capture Therapy (NCT)

In this project, the aim is to target stable ^{10}B to tumor for later activation with external neutron beams. The ^{10}B (n,α) ^{7}Li reaction provides optimal conditions for radiotherapy as the highly ionizing particles have a range of approximately 1 cell diameter, and also produce radiation damage with a high Relative Biological Effect (RBE). Preliminary studies with seven classes of compounds have demonstrated selective uptake in tumor, as well as physiological pathways with the potential for carrying therapeutic amounts of boron to tumor. In addition, boronated analogs of these compounds had previously been described in the literature. The compounds, listed roughly in order of increasing carrying capacity, are: steroids, antibodies, nucleosides, chlorpromazine, thiouracil, amino acids, and porphyrins. Boronated analogs of

steriods, nucleosides, amino acids, and porphyrins have been obtained via collaborative efforts with groups outside BNL, and are currently being tested in cell culture and in small animals. Preliminary results with boronated analogs of thymidine, phenylalanine, and tetraphenylporphinesulfate indicate biological activity as well as uptake in therapeutic amounts. As an example, single cell survival curves of hamster V-79 cells grown in the presence of the thymidine analog dihydroxyboryldeoxyuridine (DBDU) are shown in Fig. 4. The decreased survival of cells with incorporated boron (relative to "controls" with no boron) provides emphatic evidence of physiological binding, as well as evidence of uptake in quantities sufficient for therapy (the use of DBDU enriched in ^{10}B would increase the effects shown in Fig. 4 by a factor of 5). Of the seven biomolecules listed above, boronated antibodies have the greatest overall potential, since in principle they can be directed against any type of tumor with high specificity. A large effort is being directed towards synthesis of such boronated antibodies, using dextran bridges to increase boron content. Supplementary funding for this aspect of the project has been obtained from NIH[2]. Resolution of the encouraging results noted above has been made possible through physical boron microanalytical techniques (prompt-gamma, track etching) unavailable elsewhere. It is expected that continued testing will shortly result in a boronated compound showing physiological binding and a consequent tissue distribution significantly better than that of $Na_2B_{12}H_{11}SH$ currently in clinical use for NCT in Japan.

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2 1-R01-CA32920; D. C. Borg and R. G. Fairchild, Co-P.I.'s.

2. Photon Activation Therapy (PAT)

The concept of PAT is analogous to the use of a boronated nucleoside in NCT. The difference is that instead of neutrons and ^{10}B, 32 to 50 keV photons are used to stimulate radiation sensitized damage and Auger (electron) cascades via stable ^{127}I. This can be done when ^{127}I is incorporated in DNA through substitution of iodinated deoxyuridine (Idurd) for thymidine (Tyd). Theoretical analysis has shown that at five percent replacement (of Idurd for Tyd) therapeutic gain (TG) should vary from 2.2 to 17 depending on dose rate (Fig. 5). Proportionately higher gains are achieved at higher replacements. Most of the parameters used in calculating TG have been verified in cell culture using hamster V-79 cells "pulsed" for one cell cycle (12 hours) in media containing Idurd. Typical results for 40% exchange are shown in Fig. 6, which shows the effects of radiation sensitization (3A) and sensitization plus photoactivation (3B). The most important finding in these experiments has been the fact that damage from sensitization and photoactivation is evidently non-repairable, as evidenced by the lack of a "shoulder" in Fig. 6. Thus the use of protracted irradiations with implanted sources in brain tumors should produce the extraordinary therapeutic gains shown in Fig. 5 (i.e., 17.3 at 5% replacement). This follows since surrounding normal brain tissues do not synthesize DNA; thus damage from activating photons in normal brain should be mainly repairable damage. Five percent replacement of Tyd with halogenated deoxyuridine has been reported by others in human tumors.

Preliminary data in murine tumors indicate that approximately 20% replacement in vivo (average bifilar) should be possible in the proliferating cell pool. It is proposed that Sm-145 sources be used for implant therapy. These sources have been produced at BNL's High Flux Beam Reactor, from irradiation of Sm-144, and produce photons of appropriate energy (38-61 keV) upon decay by electron capture (T 1/2 = 340d). It is expected that PAT will make a significant contribution to radiotherapy. Supplementary funding for PAT has been obtained from NIH[3].

3. Thiouracil (TU)

It would be desirable to use physiological means to target radioactive nuclei directly to tumor, as in I-131 therapy of thyroid cancer. In this way it should be possible to successfully treat remote metastatic disease. Our studies with TU (which was being evaluated as a vehicle for boron transport in NCT) demonstrated a unique uptake in growing melanoma, analogous to the selective uptake of I in thyroid. TU is incorporated in melanin only as the granules are being synthesized. In adult mice and hamsters, the ratio of TU uptake in melanoma to that in normal tissues is about 100 to 1. The unique selectivity to melanoma is demonstrated in Fig. 7, which shows the distribution of C-14-TU in a mouse with melanoma, via a whole-body autoradiogram made at 4 hours (top) and 48 hours (bottom) post injection. The studies indicated that concentration of TU in tumor was high enough to permit

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3 1-R01-CA32016; R. G. Fairchild, P.I.

the delivery of therapeutic doses to tumor with commercially available S-35-TU (50 mCi/mmole). A number of mice have been treated with a total of 1.3 mCi each of S-35-TU, which should have resulted in a tumor dose of about 17 rads/hour. Results are shown in Fig. 8 (averge of four mice per point), and demonstrate a two week suppression of tumor growth. Experiments are now underway which indicate higher specific activities of S-35-TU will be more effective. It is apparent from Fig. 8 that S-35-TU should find clinical application in the treatment of primary and perhaps most importantly, metastatic melanoma. Supplementary funding for the study of TU for diagnosis and therapy has been obtained from the NIH[4].

Light Source Imaging for Diagnosis (Rubenstein, E.)

The purpose of this proposal is to conduct an evaluation of synchrotron radiation for the non-invasive assessment of coronary artery disease in human beings. The intensity and tunability of synchrotron x-ray beams provide a new source of x-rays highly-suited to the *in vivo* detection of iodine by K-edge digital subtraction angiography (DSA). The use of such beams provides maximum sensitivity to intra-arterial iodine and virtually eliminates image contrast due to non-vascular body structures. The intensity of the beams permits short exposure times and allows images to be recorded in sharp focus despite arterial motions. The sensitivity of this method to iodine offers the prospect of non-invasive visualization of the arteries by peripheral venous injection of iodinated contrast agents and, in particular, the coronary arteries.

4 1-R01-CA33725 (S. Packer and R. Fairchild, Co-P.I.'s).

The authors have already demonstrated the principles of K-edge DSA by means of inanimate phantoms, excised animal hearts, and in vivo studies in dogs. These studies have used an existing 2 cm wide x-ray beam at the Stanford Sychrotron Radiation Laboratory (SSRL). The opportunity now exists for the application of synchrotron radiation to coronary angiography in human subjects, and to angiography generally. For human subjects an x-ray beam and matching monochromator of the increased horizontal width (> 15 cm) must be provided to accommodate the size of human organs, in particular, the heart.

The optimum location in the United States for the necessary demonstration studies and subsequent first application of synchrotron x-rays to coronary angiography is the National Synchrotron Light Source (NSLS) at Brookhaven National Laboratory. A superconducting wiggler magnet at NSLS, already constructed, can provide an x-ray beam width of 23 cm at a distance of 20 meters. Moreover, the x-ray flux at 33 keV (the K-edge of iodine) provided by this wiggler is ample for angiography and is not presently exceeded elsewhere. The high duty factor of operations at NSLS is also exceedingly important to this enterprise, which can have a significant and immediate impact on a major medical problem in the United States today, namely coronary artery disease. Also important to this proposal is the presence of staff members at NSLS who wish to begin studies in this and related fields. A collaborative effort between Stanford and the NSLS personnel, strongly supported by the NSLS Director, is the most expedient way of conducting the proposed evaluation. The support of the Medical Research Department at Brookhaven, its hospital facilities, and its experience in clinical programs of evaluation are obviously of great importance.

Radiotracers for the Study of Metabolism in the Brain and Other Tissues

(Wolf, A. P. and Fowler, J.)

A new combination of techniques involving the use of radiotracers, not just to follow or locate anatomic structures within human beings, but actually to measure biochemical processes within tissue has rapidly evolved over the past ten years. Radiotracers used in this technique are positron emitters, particularly advantageous in that they are relatively easy to produce. They are isotopes of short half-life ranging from two minutes to two hours, an important factor in minimizing radiation exposure. The three most important compounds in widespread use are FDG (^{18}F-fluorodeoxyglucose) CDG (^{11}C-deoxyglucose) and ^{15}O-oxygen. Using these and other newly developed compounds, it is now possible to measure regional brain glucose metabolism, oxygen consumption, protein synthesis, neurotransmitter receptor activity and perhaps the growth rate of tumors. Similar studies can be applied to an investigation of the state of health of the heart. The analytical tool used to gather the pertinent data is PET, a Positron Emission Tomograph. Characteristics which set this new approach apart from CT, NMR and other imaging techniques is the ability to actually develop a dynamic profile of an ongoing biochemical process in normal and abnormal states.

To develop a successful treatment for a disease, a first essential step is usually to seek the underlying biological processes of the illness and of normalcy. In brain research, the PET is especially useful for the contrasting of health and disease. From PET measurements one can contrast the dynamic metabolic rates of a diseased brain with those from a set of normal brains in

order to locate and to quantify the pathological processes. Knowing the disease-affected processes, the quest for a cure or palliation can proceed on the solid ground of fact rather than on serendipity alone. An important illness of the brain provides a good example of how PET is being used in medical research.

Alzheimer's disease (AD), a prevalent form of senile dementia, is having a major impact on our society, especially as longevity in the general population is gradually increasing. It currently affects two million Americans and is the fourth leading cause of death. The absolute values of regional brain glucose metabolism measured using FDG and CDG can be related to cognitive impairment and changes in regional brain structure. Drug interventions designed to alleviate some symptoms and the state of progression of the disease can be related with changes in metabolism and other biochemical processes in the brain yielding much new information about this debilitating disease. The comparison of the metabolic patterns in a normal brain (Fig. 9) and with those of a patient with AD, (Fig. 10), clearly shows a marked reduction in glucose metabolism, in the AD patient, a metabolic change not seen in normal aging. Both the diminution of metabolic activity, where it first appears, and how it progresses can be used as disease markers. Thus the use of these labeled tracers can probe early stages of AD and provide much new information on its characteristics, which hopefully may be applied in stabilizing patients at an early stage or developing palliatives to be used in its treatment. The ultimate goal is to provide information on the causes of this disease which, when taken with research in other areas, may eventually lead to a cure.

Another major study being carried out is a systematic biochemical characterization of schizophrenia to augment the traditional behavioral characterization of the disease. Positron emitter tracers have been used to demonstrate altered metabolic rates in specific regions in chronic schizophrenic patients in the resting state and when performing certain psychological tasks, suggesting that treatment should be directed at correcting either the metabolic deficiencies or establishing compensatory mechanisms.

The application of the positron emitting radiotracers and their assay in living tissue using positron emission tomography has shown great promise in developing new understanding of some of the most baffling disorders afflicting our population. It provides the medical profession with a significant new modality for the diagnosis and evaluation of treatment of many disease states.

IMPACT OF THE FY 1985 BUDGET
ON BROOKHAVEN NATIONAL LABORATORY'S
BIOLOGICAL AND ENVIRONMENTAL RESEARCH PROGRAM

(Dollars In Thousands)

Impact	FY 1984	FY 1985	Change
Human Health Research:	2,605	560	(2,045)
• The Inhalation Toxicology Facility for exposure of small animals to respiratory toxicants, and the Large Animal Facility for carrying out studies closely related to human inhalation toxicology and pulmonary biology will have to be closed. Integrated studies in large animal/human pulmonary research will be reduced to a skeleton program. The combined impact of budget reductions in this category and in Nuclear Medicine Applications requires shutting down the in-patient research hospital.			
Health Research in Biological Systems:	4,780	4,354	(426)
• There will be a decrease in efforts to correlate decreases in DNA repair with carcinogenic risks associated with environmental agents. • There will be a decrease in the basic scientific work on mutagenesis needed for a quantitative understanding of the mutagenic action of energy related pollutants. • There will be a decrease in the biological research and development at the unique national facilities for structural biology (HFBR and NSLS). There is not only a serious shortfall in operating money but the funds available for instrumentation to make these facilities available to university and industrial users are only one-third of what is needed. • The program on carcinogenicity associated with hemopoietic regulation (leukemogenesis), an energy-related occupational and environmental health effect of great current concern, and the program on chemical and radiation-induced carcinogenesis will both be terminated. • The program on the hazards of radioactive environmental pollutants will be severely curtailed, especially the project on tritium toxicity, and the programs on molecular cytogenetics and genetic toxicology monitoring will be reduced.			
Environmental Research:	1,859	1,759	(100)
• The research and development in this area also is in the field of structural biology (NSLS and our unique Scanning Transmission Electron Microscope). The operating and capital funds for these projects are approximately 20% below what is needed to make the instruments involved readily available for research by university and industrial users.			

IMPACT OF THE FY 1985 BUDGET
ON BROOKHAVEN NATIONAL LABORATORY'S
BIOLOGICAL AND ENVIRONMENTAL RESEARCH PROGRAM

(Dollars In Thousands)

Impact	FY 1984	FY 1985	Change
Physical and Technological Research:	2,577	3,802	1,225
• This increase is insufficient to support the level necessary to meet deadlines imposed in the important national acid rain program.			
Carbon Dioxide Research:	300	100	(200)
• The work on carbon storage and pollution export, which is important to the understanding of the global carbon cycle and energy-related impacts will be terminated.			
Health and Environmental Risk Analysis:	527	0	(527)
• The Assessment of Health Effects, which provides an important integrative link to DOE health and safety programs will be terminated. It is critical that such health and safety information be provided in a risk assessment format for both decision maker and research use.			
Nuclear Medicine Applications:	4,976	4,886	(90)
• Failure to maintain the FY 1984 level of effort will seriously impact our leading program in medical physics and continuation of animal studies supported in this research category on the leukemogenesis of benzene, a major occupational and environmental pollutant of great current concern.			
TOTAL, BNL/Biological and Environmental Research Program	17,624	15,461	(2,163)

The FY 1985 Biological and Environmental Research Program budget for BNL, after deducting an increase of $2,080,000 for the Acid Rain program and allowing for the effects of inflation, represents an effective decrease of approximately 25% in funding. This will result in a reduction of about 68 scientific and supporting staff. Because of stringent budgets over the last several years, the FY 1985 budget is particularly devastating in that it begins to bring into question the viability of the program.

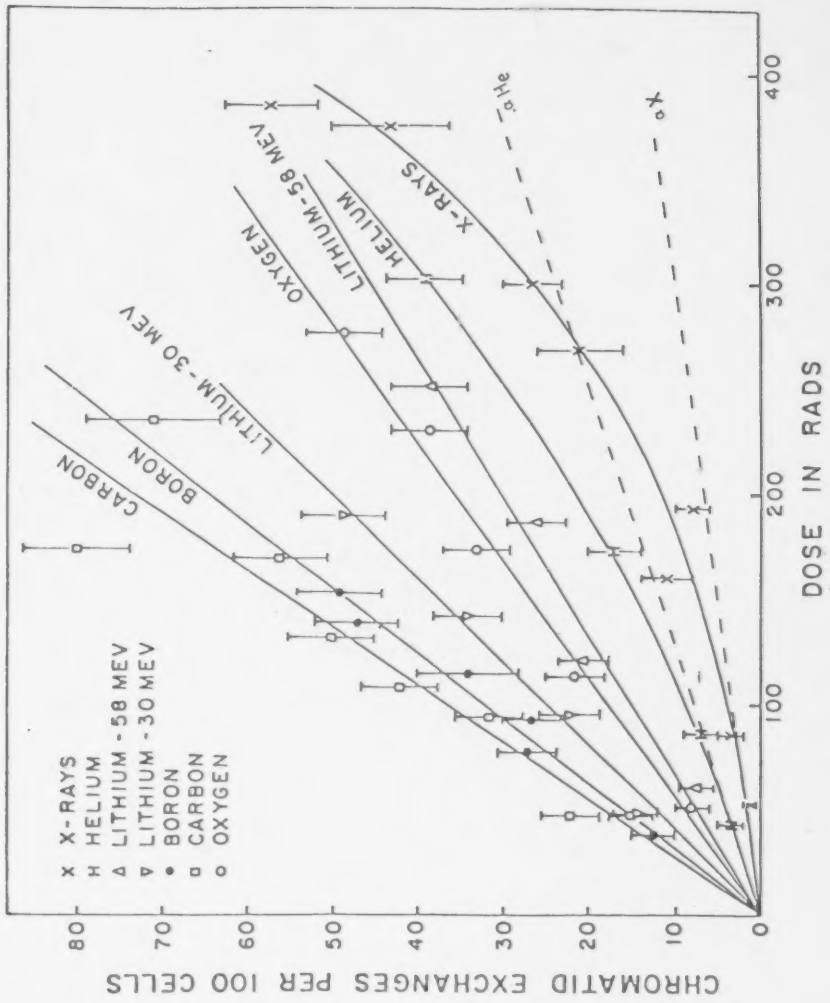

CHROMATID EXCHANGES PER 100 CELLS
DOSE IN RADS
0
10
20
30
40
50
60
70
80
100
200
300
400
X-RAYS
HELIUM
LITHIUM-58 MEV
OXYGEN
LITHIUM-30 MEV
BORON
CARBON
X - RAYS
α-He
X HELIUM
Δ LITHIUM - 58 MEV
▽ LITHIUM - 30 MEV
• BORON
□ CARBON
○ OXYGEN

FIG. 1

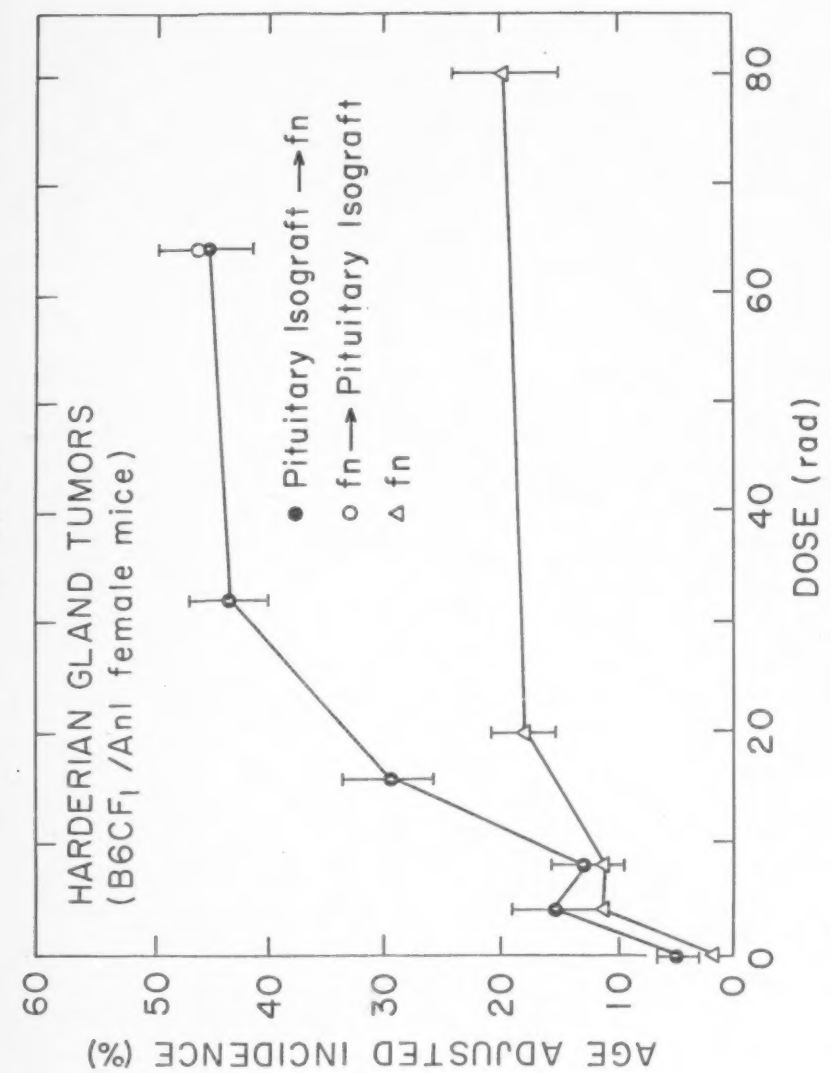
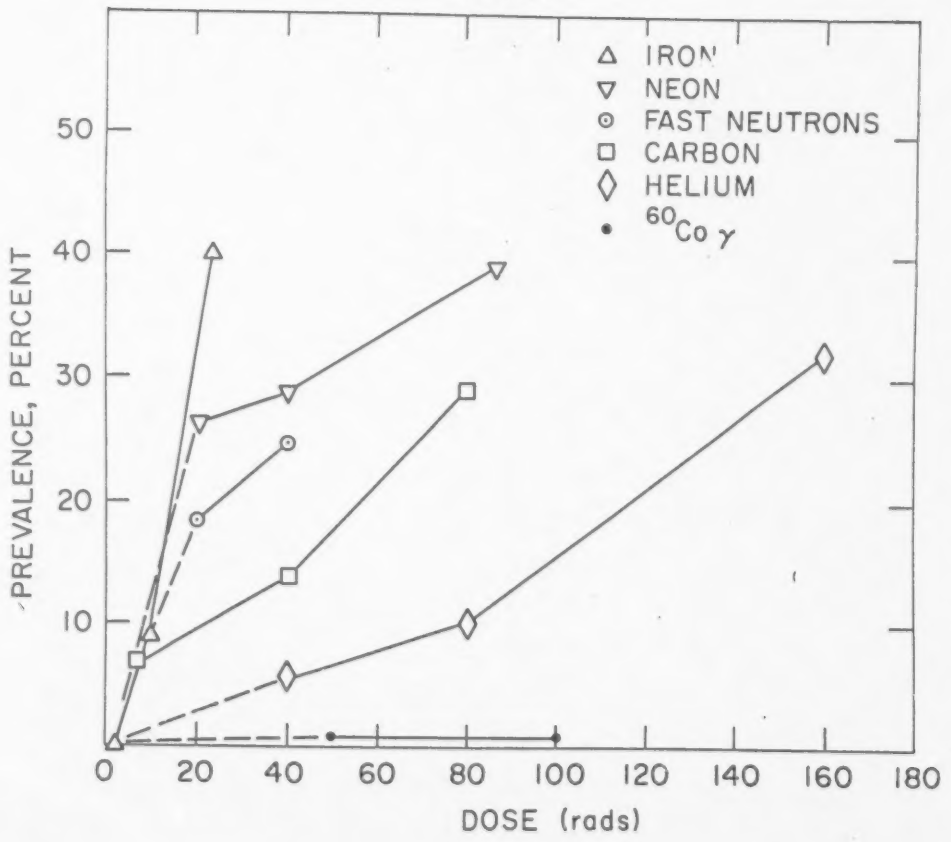


Fig. 2

36-326 O - 84 - 6

FIG. 3



BOND
11-668-81

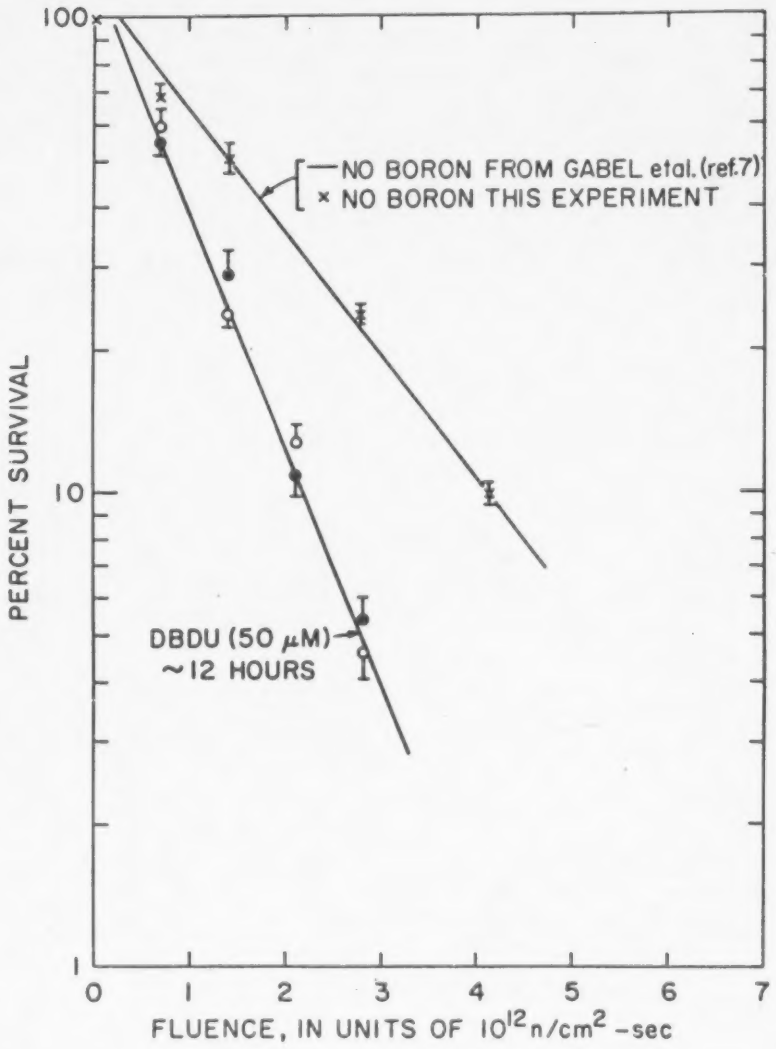

100
10
1
PERCENT SURVIVAL
NO BORON FROM GABEL etal. (ref.7)
× NO BORON THIS EXPERIMENT
DBDU (50 μM)
~12 HOURS
0
1
2
3
4
5
6
7
FLUENCE, IN UNITS OF 10^{12} n/cm^2 -sec

FIG. 4

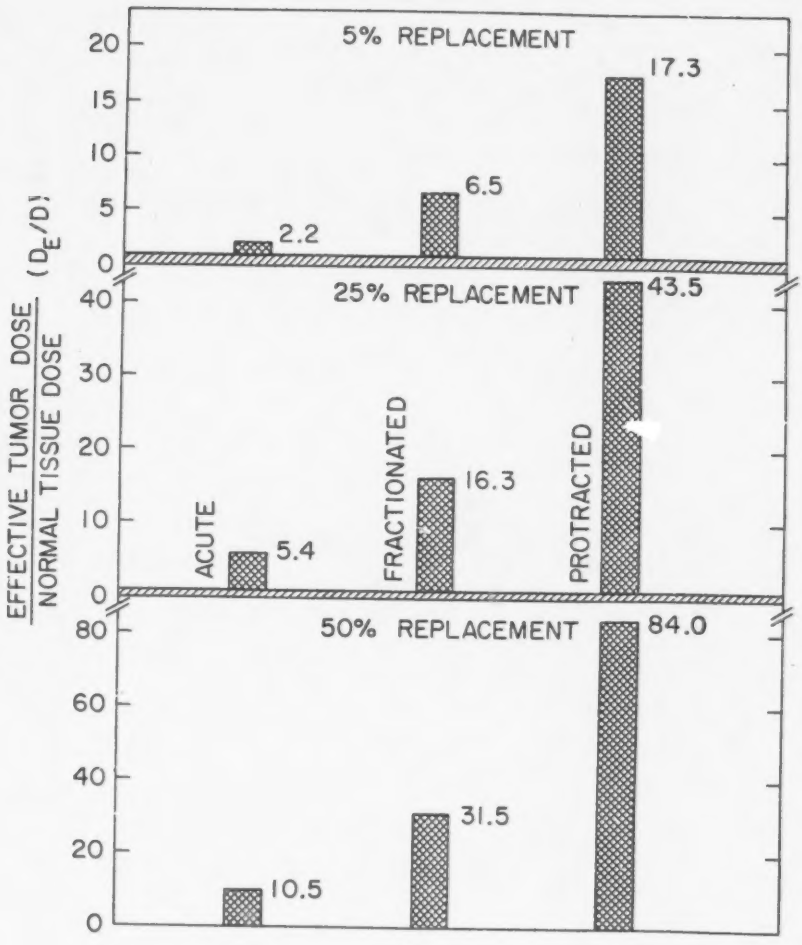

5% REPLACEMENT
17.3
6.5
2.2
25% REPLACEMENT
43.5
16.3
5.4
50% REPLACEMENT
84.0
31.5
10.5
ACUTE
FRACTIONATED
PROTRACTED
EFFECTIVE TUMOR DOSE / NORMAL TISSUE DOSE (DE/D1)
0
5
10
15
20
30
40
60
80

FIG. 5

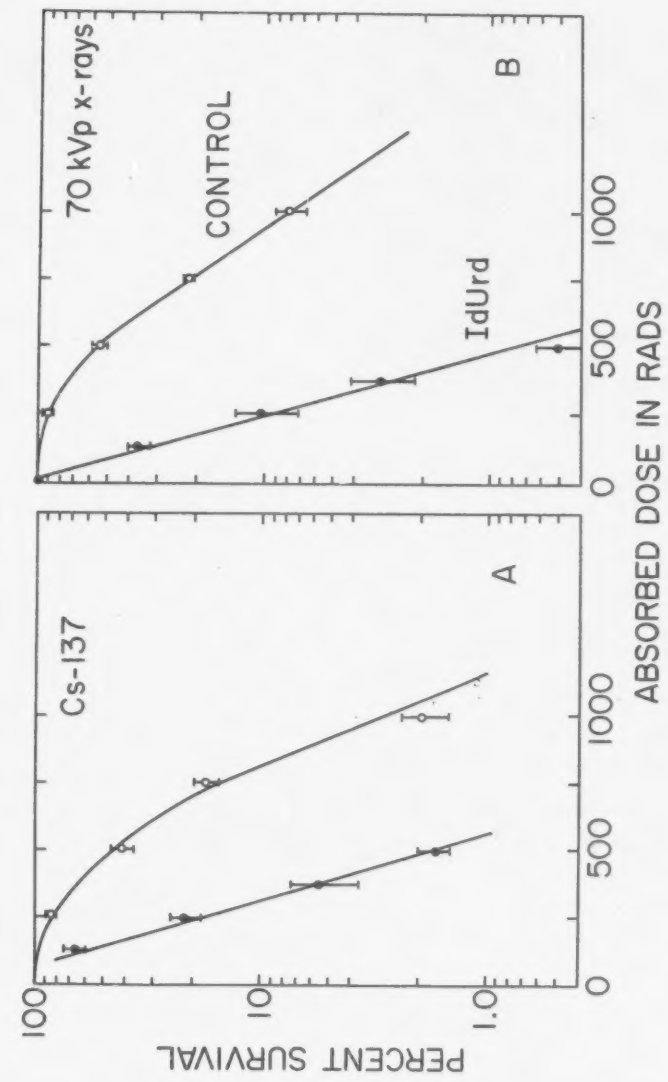

70 kVp x-rays
CONTROL
IdUrd
B
Cs-137
A
100
10
1.0
0
500
1000
0
500
1000
PERCENT SURVIVAL
ABSORBED DOSE IN RADS

FIG. 6

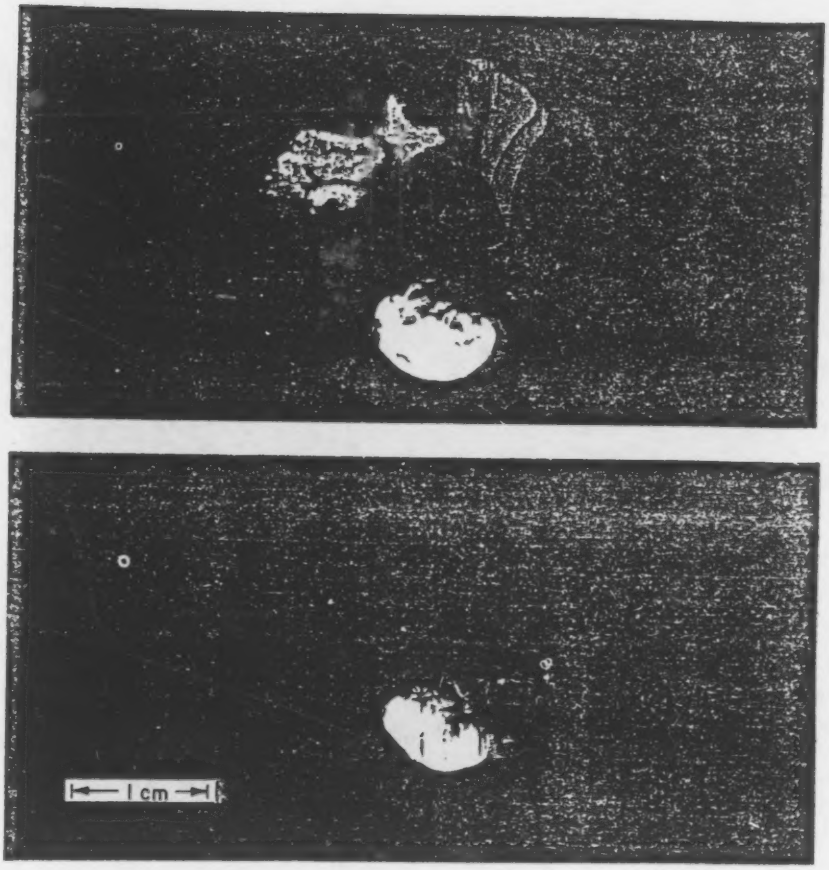


FIG. 7

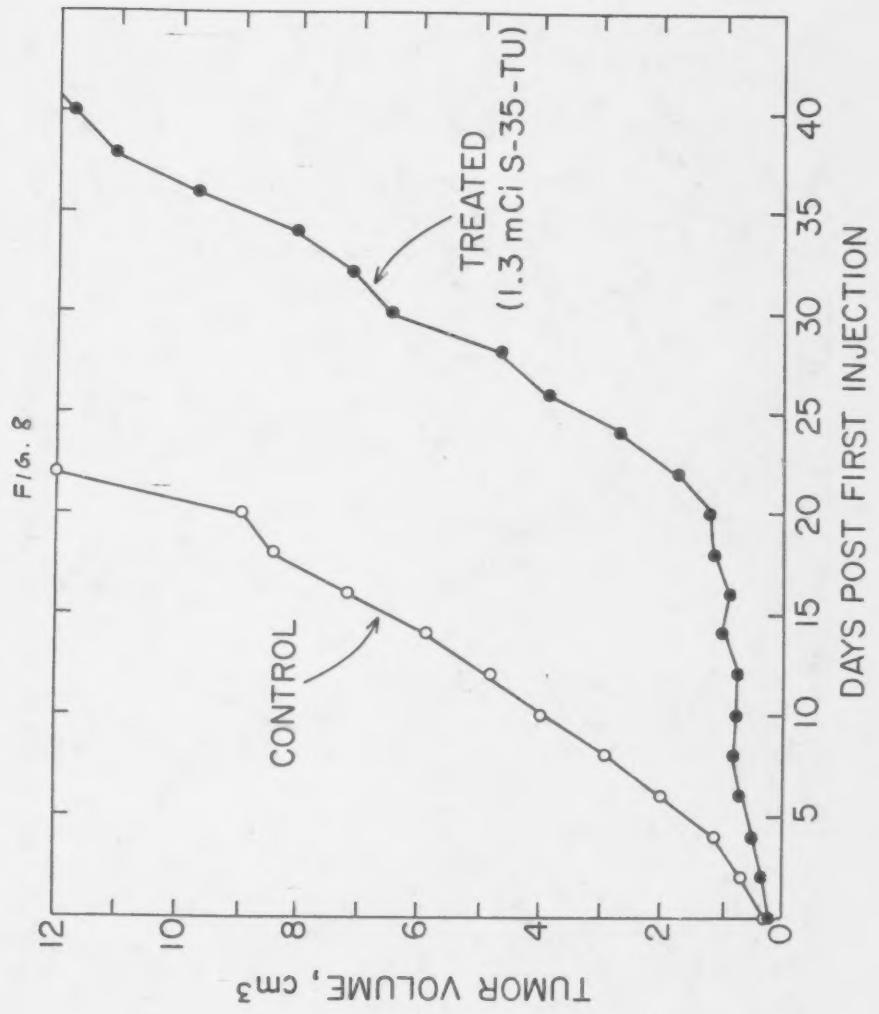

TUMOR VOLUME, cm³
0
2
4
6
8
10
12
5
10
15
20
25
30
35
40
DAYS POST FIRST INJECTION
TREATED
(1.3 mCi S-35-TU)
CONTROL

FIG. 8

FIG. 9

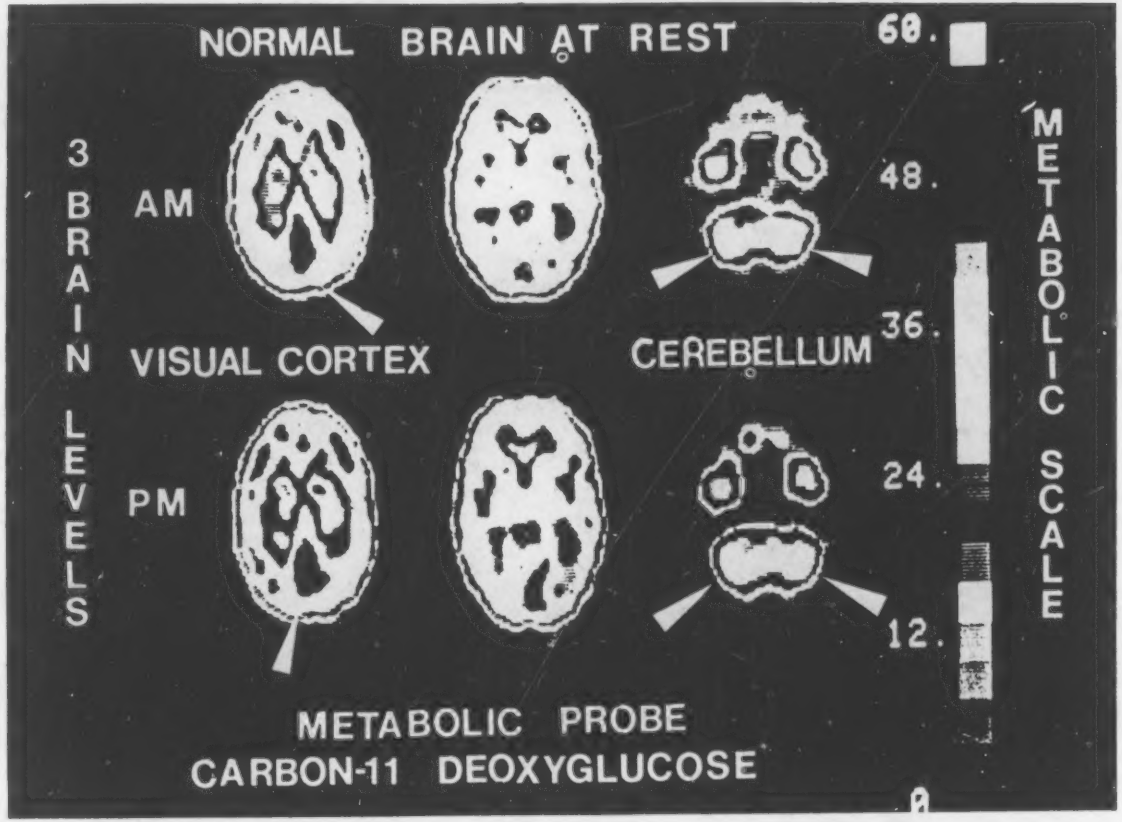
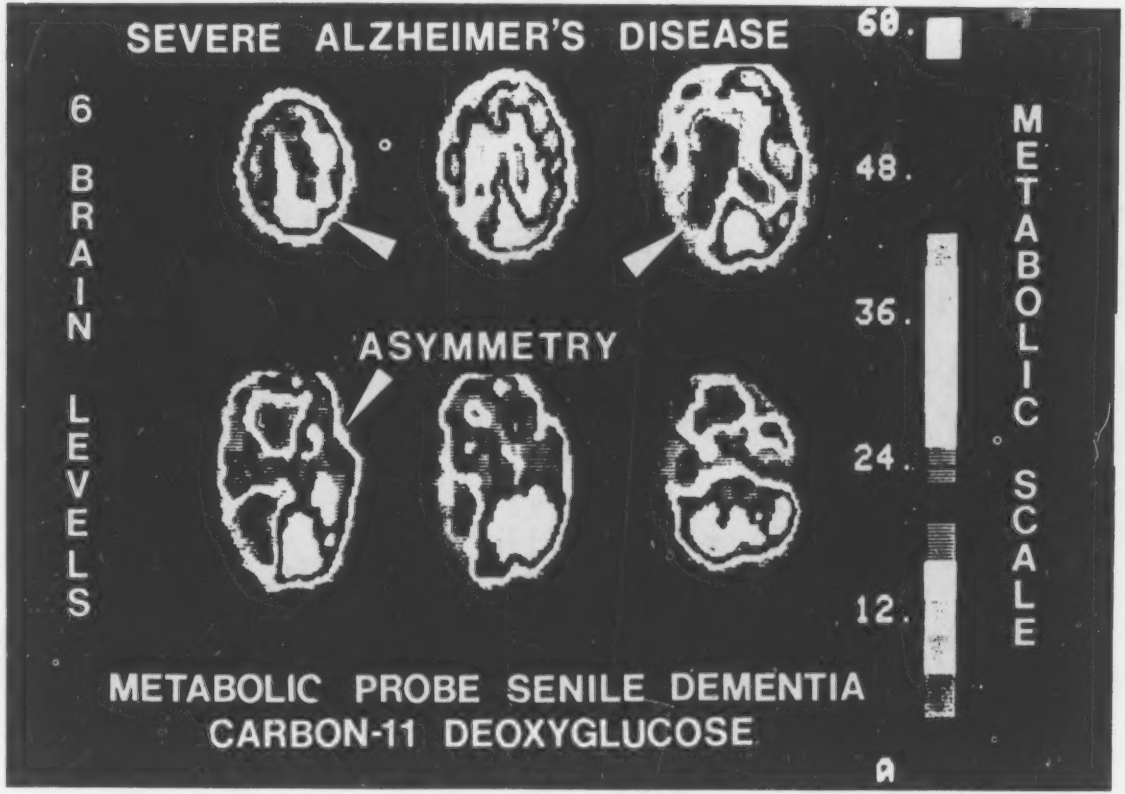

NORMAL BRAIN AT REST
3 BRAIN LEVELS
AM
PM
VISUAL CORTEX
CEREBELLUM
60.
48.
36.
24.
12.
0
METABOLIC SCALE
METABOLIC PROBE
CARBON-11 DEOXYGLUCOSE

FIG. 10


SEVERE ALZHEIMER'S DISEASE
6 BRAIN LEVELS
ASYMMETRY
60.
48.
36.
24.
12.
METABOLIC SCALE
METABOLIC PROBE SENILE DEMENTIA
CARBON-11 DEOXYGLUCOSE

November 1983

BIOGRAPHICAL SKETCH

Victor P. Bond

Born: Santa Clara, California, 30 November 1919

Education: University of California, Berkeley, A.B., 1943
University of California, San Francisco, M.D., 1945
University of California, Berkeley, Ph.D., Medical Phys., 1952
Long Island University, New York, Honorary D.Sc., 1965

1. Positions:

Associate Director (for Biology, Medicine, Environment, and Safety)
Brookhaven National Laboratory,
Upton, New York, April 1967 - present

Adjunct Professor of Radiology
Columbia University, 1969 - present

Professor of Medicine
Health Sciences Center
State University of New York
at Stony Brook, 1968 - present

Chairman, Medical Department
Brookhaven National Laboratory,
Upton, New York, 1962 - April 1967

Head, Division of Microbiology,
Medical Research Center,
Brookhaven National Laboratory, 1957-1962

Scientist, Medical Research Center,
Brookhaven National Laboratory,
Upton, New York, 1955-1957

Head, Experimental Pathology Branch,
U. S. Naval Radiological Defense
Laboratory, San Francisco, California,
1948-1954

2. Fields of Interest:

Medicine, hematology, radiation biology, nuclear medicine

3. Present Activities:

Chairman, NCRP Scientific Committee 40 on Biological Effects of Radiation

Chairman, NCRP Scientific Committee 71 on the Probability of Radiogenic Cancer Causation

Member, Scientific Committee 75 on Guidance on Radiation Received in Space Activities

Member, Committee I of ICRP, on Biomedical Effects of Radiation

Member, Committee I of NCRP on Biomedical Effects of Radiation

Member, Three Mile Island, Advisory Panel on Health Research Studies, Pennsylvania Department of Health

Member, Advisory Group, NAS Committee to Revise the NRC's Radiological Health Effects Model

Consultant, Public Health Service, Department of Health, Education and Welfare

Consultant, Defense Atomic Support Agency

4. Earlier Activities and Information

Participant and project officer in biological work involving field testing; deputy director of the medical team that cared for the Marshallese following exposure to fallout radiation in 1954.

Former member of:

Board of Directors, Radiation Effects Research Foundation (formerly ABCC), Hiroshima, Japan
Life Sciences Committee, NASA
Committee on Radiobiology, American College of Radiology
Panel for Assessing the Biological Hazards of Ionizing Radiation for Space Workers, Satellite Power System, NASA

4. continued

Public Health and Safety Task Force of the President's Commission on the Accident at Three Mile Island
National Advisory Committee on Radiation
Subcommittee on Radiological Dosimetry, ICRU
Ad Hoc Committee on RBE; ICRP and ICRU
Armed Forces Panel on Radiological Instruments
Scientific Advisory Board, USAF
Committee on Nuclear Science, NAS
Committee for Radiation Bio-aspects of SST, FAA
Board of Directors, NCRP
Commission on Epidemiological Survey, AFEB, DOD
Radioactive Pharmaceuticals Advisory Comm., FDA
Advisory Committee of the FRC (part of EPA) NAS
Biological Effects of Ionizing Radiation (BEIR I Committee), NAS/NRC

Former Chairman of:

ICRU Committee 10e on Biological Dosimetry
Subcommittee M-4 of the NCRP, on Relative Biological Effectiveness
Radiation Bio-effects Advisory Comm. for the Div. of Radiological Health (DHEW)
Radiation Study Section, NIH, DHEW
Subcommittee on Radiobiology, Committee on Nuclear Science, NAS
Director, Commission on Radiation Infection AFEB
Vice President, then President, Radiation Research Society
President, 5th International Congress of Radiation Research, Seattle, 1974

5. Publications

Author or co-author of over 300 articles in the fields of radiation biology, hematology, cell kinetics, radiation risks and experimental radiotherapy.

Mr. SCHEUER. Thank you very much.
Dr. Warren Sinclair.

STATEMENT OF DR. WARREN K. SINCLAIR, NATIONAL COUNCIL ON RADIATION PROTECTION AND MEASUREMENT, BETHESDA, MD

Dr. SINCLAIR. Thank you, Mr. Chairman.
Mr. SCHEUER. If you would try to hold it to about 6 or 7 minutes.
Dr. SINCLAIR. I will try to do so, sir.

I am the president of the National Council on Radiation Protection and Measurements and I need to explain something about that council for you to understand where I'm coming from. It's a private, not-for-profit corporation; it's chartered by the Congress of the United States, and it publishes reports on all aspects of radiation protection.

The council has 75 members, and there are about 500 additional members who serve on its committees. And they produce reports like these—on radiation biology, the effects of dose and dose rates, on things that expose people, the natural background in the United States, its magnitude, the sources it comes from, and so on. On guidance in radiation protection, pediatric radiology, and others like it in nuclear medicine, and so on. Reports having to do with the nuclear power program, one of the residuals of the nuclear power program, krypton-85, how much of it, what does it do, and so on. A corollary to that which turned out to be useful at Three Mile Island, krypton-85——

Mr. SCHEUER. Dr. Sinclair, our time really is tight this afternoon. If you could give us just the main nub of your testimony in about 5 or 6 minutes remaining, we'd be very grateful.

Dr. SINCLAIR. OK.

Well, because NCRP reports assess the state of knowledge in a field, we feel we are in a particularly good vantage point to survey the status of that knowledge. In the case of radiation protection, what we need to know are the effects of low doses on people. Some of that information we get directly from people, and there's a list in the first of your illustrations there of the sources of information about people. Any such list is headed by the Japanese survivors of the atomic bombs, because they provide by far the greatest amount of information, but not the only amount. The study of the survivors of the atomic bombs has been going on now since shortly after 1945, and the information is still accumulating in a very important way. And the second illustration shows you how the solid tumors in those people are still increasing, whereas the leukemia has decreased.

We have also recently undertaken a reinvestigation of the doses to which those people were exposed, 40 years later, and measurements are being made that can still tell us what those doses were—better now than at the time. Those investigations, and the importance of them to radiation protection, are inestimable because they provide us with very much of our human information. And the program, of course, that I'm referring to, the investigation of the Japanese, has been supported from the Department of Energy's OHER

Program from its outset. And we still participate with the Japanese in those investigations.

Well, as important as the epidemiological studies are, they have weaknesses; and one of their limitations is that we usually obtain information of doses much higher than those that we want to use, in hundreds of rad range rather than the 1-to-10 rad range where people are exposed, either occupationally or to public sources. So one of our problems is extrapolating downwards from the information we've got in human beings to the levels that we're interested in. We do that with the help of studies in the laboratory on dose effect relationships which give us information on how to get from the high doses, where we know what the effects are, to the low doses, where we're interested in describing what the effects are. That work comes from the laboratory in a whole variety of animal systems.

In addition, there are many areas of radiation effects work in which we don't have human information at all. There are three outstanding examples of that, and probably many more, but three I've cited in my testimony. One has to do with genetic effects where we rely entirely on the work that was done at Oak Ridge National Laboratory and is still being done, because we have no human information in the case of genetic effects, and in the effects of internal emitters like plutonium. Our information is very limited on the human side, and most of what we know comes from comparisons with radium in animal systems in the DOE laboratories.

And finally, on the effects of high-LET radiation, the penetrating radiation of neutrons which was mentioned earlier as being used for therapy. Again, we have no human information. And these neutrons are part of the scene, occupationally; they don't expose as many people as the low-LET radiations do, where we have something like 1.3 million people in this country exposed, potentially, occupationally, to low-LET radiation; but 40,000 or 50,000 of them are potentially exposed to the neutrons in and around reactors and other places where neutrons are produced. And although we know that neutrons are potentially substantially more hazardous than x rays and gamma rays, we don't know exactly by how much, and especially at low doses we don't know by how much. And the studies that are presently being conducted, for example with the JANUS reactor at the Argonne National Laboratory on tumor induction and life shortening in mice and on transformation in cultured mammalian cells, are enabling us for the first time to reach down to the lowest doses of interest in the neutron occupational exposure field. And we're finding—we're not sure of this yet, because the information is not definite—that instead of the 10 times or so that we thought neutrons were more effective than x rays and gamma rays, the real number may be more like 20 to 70, and we're trying to find out more about that now in the laboratory because without human information, our levels, our standards for neutrons, must depend on these laboratory studies.

Mrs. Schneider, the NCRP has been producing reports relating to radiation protection for many years, and the great majority of the information we have has come from studies supported by DOE-OHER. Many of these have been careful, painstaking, long-term studies in animal systems, some of which are only now becoming

fully fruitful. Many other investigations must be undertaken and exploited as new information indicates new directions. Such studies are vitally important, not only to our own national interests, but as part of the larger sphere of necessary scientific knowledge at the international level. The United Nations Scientific Committee on the effects of atomic radiation, the International Commission on Radiological Units, and the International Commission on Radiological Protection all depend on past and future scientific work supported by DOE-OHER just as we at the National Council do.

I cannot emphasize too strongly the need we see for the continuing acquisition of information in this area and the importance of stable, adequate funding in radiation carcinogenesis and related studies to ensure that our knowledge of low-dose radiation effects will continue to improve and that the United States will maintain a strong position in matters of radiation protection. Thank you.

[The prepared statement of Dr. Sinclair follows:]

TESTIMONY BY

WARREN K. SINCLAIR

My name is Warren Keith Sinclair. I reside at 2900 Ascott Lane, Olney, Maryland, and I have a Ph.D. in Physics and a background in biophysics and radiobiology. I am the President of the National Council on Radiation Protection and Measurements, a private, not-for-profit corporation, chartered by the Congress of the United States, which publishes reports on all aspects of radiation protection.

The Council has 75 members, all experts in their field, and embracing a wide range of disciplines in science, medicine and engineering, including specialists in non-ionizing as well as ionizing radiation. In addition, there are about 500 scientists involved in the work of the 70 or so committees and task groups that are presently active in the NCRP. All of these persons serve voluntarily. The organization is supported by about 40 collaborating organizations, mainly scientific and medical societies, but including various branches of the federal government and the armed services.

The NCRP produces scientific reports on a wide variety of topics that relate to radiation protection, including, for example:

- radiobiology, like Report No. 64 (1),
- assessment of dose to the public, like from natural background, Report No. 45 (2),
- guidance, as for example in pediatric radiology, Report No. 68 (3),
- on information, as for example, Report No. 44 on krypton-85 (4),
- and its corollary, a report on krypton-85 venting at Three Mile Island (5),
- and lastly, for the present, on non-ionizing radiation (microwaves) in Report No. 67 (6).

These reports are produced carefully, initial work being done by a drafting committee of experts appointed by the Board of Directors of the NCRP, followed by critical review by other Council experts, and finally, a review by all 75 members of the Council. About 1.3 million copies of these reports have been sold or distributed, and they constitute an important base of knowledge in the radiation protection field.

Because NCRP reports assess the state of knowledge in various phases of radiation protection work, at the NCRP we have an almost unique vantage point to survey the status of our knowledge of the effects of radiation on living

systems as it relates to radiation protection. While we have, fortunately, learned a great deal about radiation effects in the past 30 years or so, there are still many important unresolved scientific problems that limit our understanding of the mechanisms involved and, therefore, limit our confidence in the levels we feel need to be applied for adequate protection. I shall concentrate here on the effects of ionizing radiation.

What we need in order to make sound reasonable recommendations about protection levels and procedures is an adequate knowledge of the effects of low doses of ionizing radiation on human beings. We have some direct information on this from epidemiological studies in irradiated people and this information is widely and carefully studied. (List of sources of information -- Viewgraph 1) One of the most important sources here is the Japanese populations exposed at Hiroshima and Nagasaki to atomic bombs in 1945 who have been studied closely ever since and who are just now showing marked increases in solid tumor incidence, especially tumors of the lung, breast, G.I. tract, etc. (Viewgraph 2 on solid tumor incidence vs. leukemia) In addition, as many here may be aware, a re-investigation of the Japanese dosimetry in the last two or three years is showing some significant and important differences in the exposures at Hiroshima from what we previously thought. Although these investigations are still in progress, they have already modified somewhat our knowledge of gamma-ray risks and negated some apparent information we thought we had on the effects of neutrons. The development of the accumulating information on tumor incidence and the outcome of the re-investigations of the dosimetry are awaited with great interest, worldwide, by every national and international group or body, including the United Nations, concerned with risk and radiation protection. These investigations of the Japanese have, from the outset, been supported by the DOE-OHER program, as indeed have some other important epidemiological studies.

Epidemiological sources of information are of tremendous importance, and every one of them must be exploited as unique opportunities to gain important information on radiation effects in man, and their dependence on age, sex, etc., but they have limitations, the most important of which is probably the fact that most of the data are obtained at relatively high doses, 50-100 rads and more, whereas the important levels of low dose exposure are perhaps 1-10 rads or less, to people occupationally exposed and to the public generally

36-326 O - 84 - 7

(Viewgraph 3) from background sources, from indoor radon and from medical exposure. (Viewgraph 4)

Thus, to assess risks to humans, we must extrapolate downwards from the higher dose levels where effects are observed, to those levels where we want to use the information. This we do by means of dose effect relationships, and there are substantial arguments about the shape of these relationships, whether linear, linear-quadratic or quadratic, for example. (Viewgraph 5) Most of the information we have on what those dose effect relationships may be like come from laboratory studies in a wide variety of animal, plant and other biological systems. They are summarized, for example, in Report No. 64 of the NCRP (1). Results vary with the biological system and the circumstances, but dose and dose rate factors to account for the difference in effects between high and low doses are cited in Report No. 64 as falling in the range of 2 to 10 (1). Similar factors of 2 to 2-1/2 were used by the UNSCEAR Committee in 1977 (7) and the BEIR Committee of 1980 (8) in making their "best" estimates of the risks to human beings at low doses. Thus, while opinions about how to use the data and to make the extrapolations still differ, our knowledge of the risks of low-LET radiation (x and gamma rays and beta particles) are based on a fairly sound base of human epidemiological data, which is constantly growing, supported by broadly based knowledge of dose effect relationships in a wide variety of animal and other biological systems.

There are a number of important aspects of radiation effects in which direct human information is either lacking or limited, and we must rely either totally or mainly on laboratory studies for our information relevant to protection levels; laboratory studies which most often have been and are being conducted with support from DOE-OHER. Important examples are in genetic effects, on which we rely virtually solely on the important work in the mouse performed by Russell and his colleagues at Oak Ridge, in the effects of some internal emitters such as plutonium where laboratory studies and comparisons with radium provide most of what we presently know, and finally on the effects of penetrating high-LET radiation such as neutrons.

Let me say a little more, by way of example, about the special problems of neutrons produced in and around reactors and in some other circumstances. While these are not nearly as prevalent a problem occupationally as are low-LET x and gamma radiations, perhaps some 40-50,000 people are potentially

exposed to them. Although we know neutrons are substantially more hazardous per rad than are x or gamma rays, and we have employed a "quality factor" of 10 for this, unfortunately, we do not have a good measure of the exact relative hazard of these neutrons at low doses, partly because of the complexities of the dose effect curves in both low- and high-LET cases. (Viewgraph 6) This indicates not only that the curves are of substantially different shape, but that fractionated neutrons may be more effective than single doses, while for x or gamma rays, fractionated doses are always less effective. Some of this information has only very recently become available to us as laboratory studies have been extended to lower and lower doses.

Recent studies using the JANUS reactor at Argonne National Laboratory on tumor induction and life shortening in mice and on transformation in cultured cells seem to indicate that at low fractionated doses, neutrons may be 20-70 times more effective than x or gamma rays, depending to some extent on the circumstances of exposure, but in any case, probably substantially more than the ratio of 10 we have previously used between neutrons and gamma rays.

Recognizing the potential of increased hazard from neutron exposure, the NCRP issued a warning statement about neutrons in 1980 (9). As indicated above, very recent developments in the dosimetry of the A-bomb survivors have exacerbated the problem of understanding neutron effects, since we now appear to have no direct human information.

Thus, for high-LET neutron effects, we are totally dependent on laboratory studies, studies which themselves must proceed by building knowledge step by step and where the investigations, even in the laboratory, are quite difficult to extend down to the low doses of practical interest.

Mr. Scheuer, the NCRP has been producing reports relating to radiation protection for many years, and the great majority of the information we have depended on has come from studies supported by the DOE-OHER, as a check on the references cited would amply verify. Many of these have been careful, painstaking, long-term studies in animal systems, which are only now becoming fully fruitful. Many other investigations must be undertaken and exploited as new information indicates new directions that may lead to greater understanding of the effects of low doses of ionizing radiation. Such studies are vitally important, not only for our own national interests, but as part of the larger sphere of necessary scientific knowledge at the international level. The

United Nations Scientific Committee (UNSCEAR), the International Commission on Radiological Units, and the International Commission on Radiological Protection all depend on past and future scientific work supported by the DOE-OHER program just as we do.

I cannot emphasize too strongly the need we see for the continuing acquisition of information in this area, and the importance of stable, adequate funding in radiation carcinogenesis and related studies to ensure that our knowledge of low-dose radiation effects will continue to improve and that the United States will maintain a strong position in matters of radiation protection.

References

(1) NCRP Report No. 64. Influence of Dose and its Distribution in Time on Dose Response Relationships for Low-LET Radiations. National Council on Radiation Protection and Measurements, Bethesda, Md., 1980.

(2) NCRP Report No. 45. Natural Background Radiation in the United States. National Council on Radiation Protection and Measurements, Bethesda, Md., 1975.

(3) NCRP Report No. 68. Radiation Protection in Pediatric Radiology. National Council on Radiation Protection and Measurements, Bethesda, Md., 1981.

(4) NCRP Report No. 44. Krypton^{85} in the Atmosphere -- Accumulation, Biological Significance and Control Technology. National Council on Radiation Protection and Measurements, Bethesda, Md., 1975.

(5) NCRP Document, "Krypton^{85} in the Atmosphere -- with Special Reference to Controlled Releases at TMI." National Council on Radiation Protection and Measurements, Bethesda, Md., 1980.

(6) NCRP Report No. 67. Radiofrequency Electromagnetic Fields. National Council on Radiation Protection and Measurements, Bethesda, Md., 1981.

(7) UNSCEAR 1977. Sources and Effects of Ionizing Radiation. United Nations Scientific Committee on the Effects of Atomic Radiation. United Nations, New York, 1977.

(8) BEIR 1980. The Effect on Populations of Exposure to Low Levels of Ionizing Radiation: 1980. National Academy of Sciences, Washington, D.C., 1980.

(9) NCRP 1980. NCRP Statement on the Dose Limit for Neutrons. National Council on Radiation Protection and Measurements, Bethesda, Md., 1980.

Illustrations

Viewgraph	Slide No.	Description
1	W80-17	List of sources of human epidemiological information
2	82-24	Increase of solid tumors vs. time in Japanese, compared with leukemia
3	83-41	Occupational exposures in the USA 1980
4	84-01	Exposure of the Public
5	W80-31	Dose effect relationships showing extrapolation down
6	83-43	Dose effect relationships for neutrons vs. gamma rays

SOURCES OF HUMAN EXPOSURE INFORMATION

Japanese Survivors of A-Bombs

Marshall Islanders Exposed to Fallout

Pelvic Radiotherapy

Spinal Radiotherapy (Ankylosing Spondilitis)

Neck and Thyroid Radiotherapy

Scalp Irradiation (tinea capitis)

Breast Radiotherapy

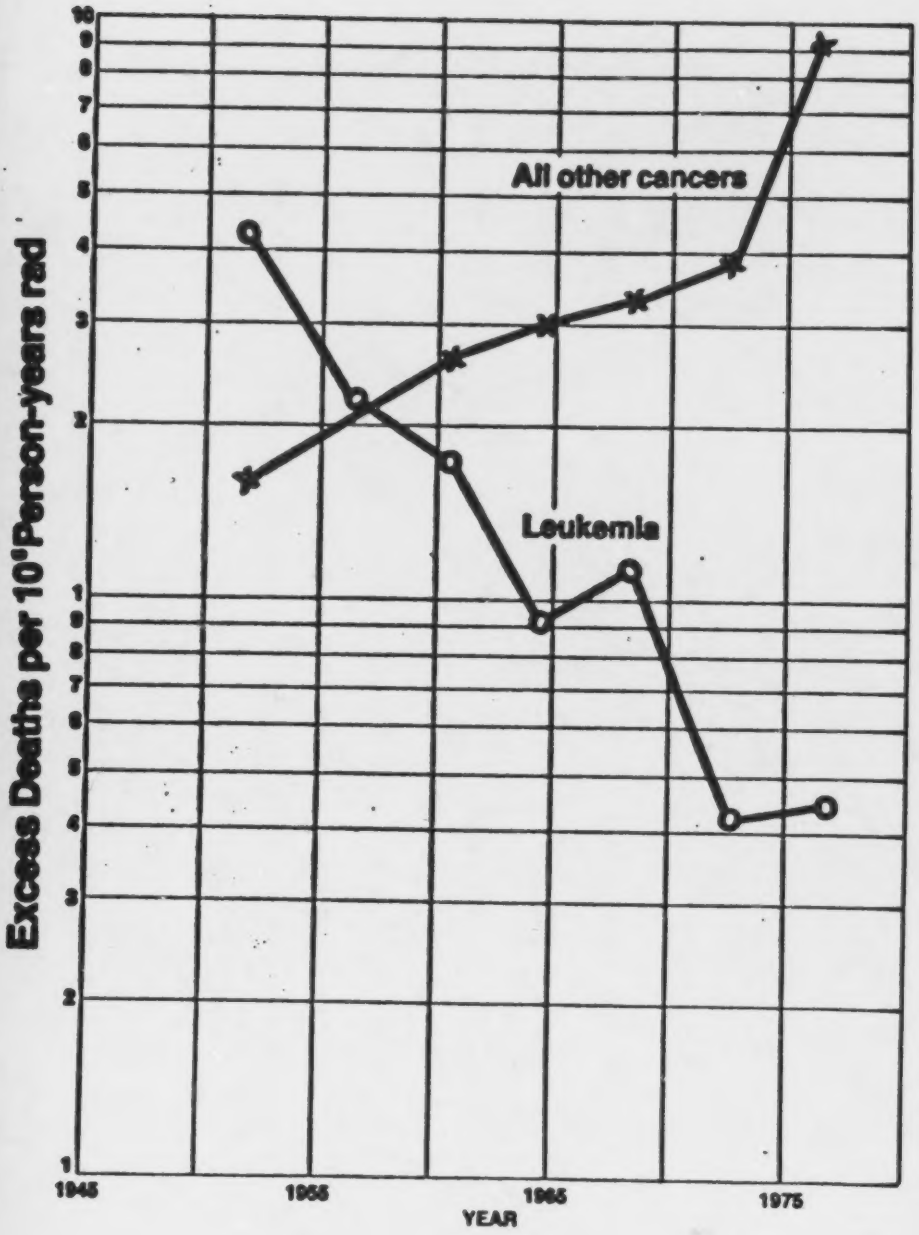
Multiple Fluoroscopies

Uranium Miners

$Radium^{226}$ Ingestion

$Radium^{224}$ Treatment

1


All other cancers
Leukemia
Excess Deaths per 10⁴ Person-years rad
1945
1955
1965
1975
YEAR

2

OCCUPATIONAL EXPOSURE SUMMARY

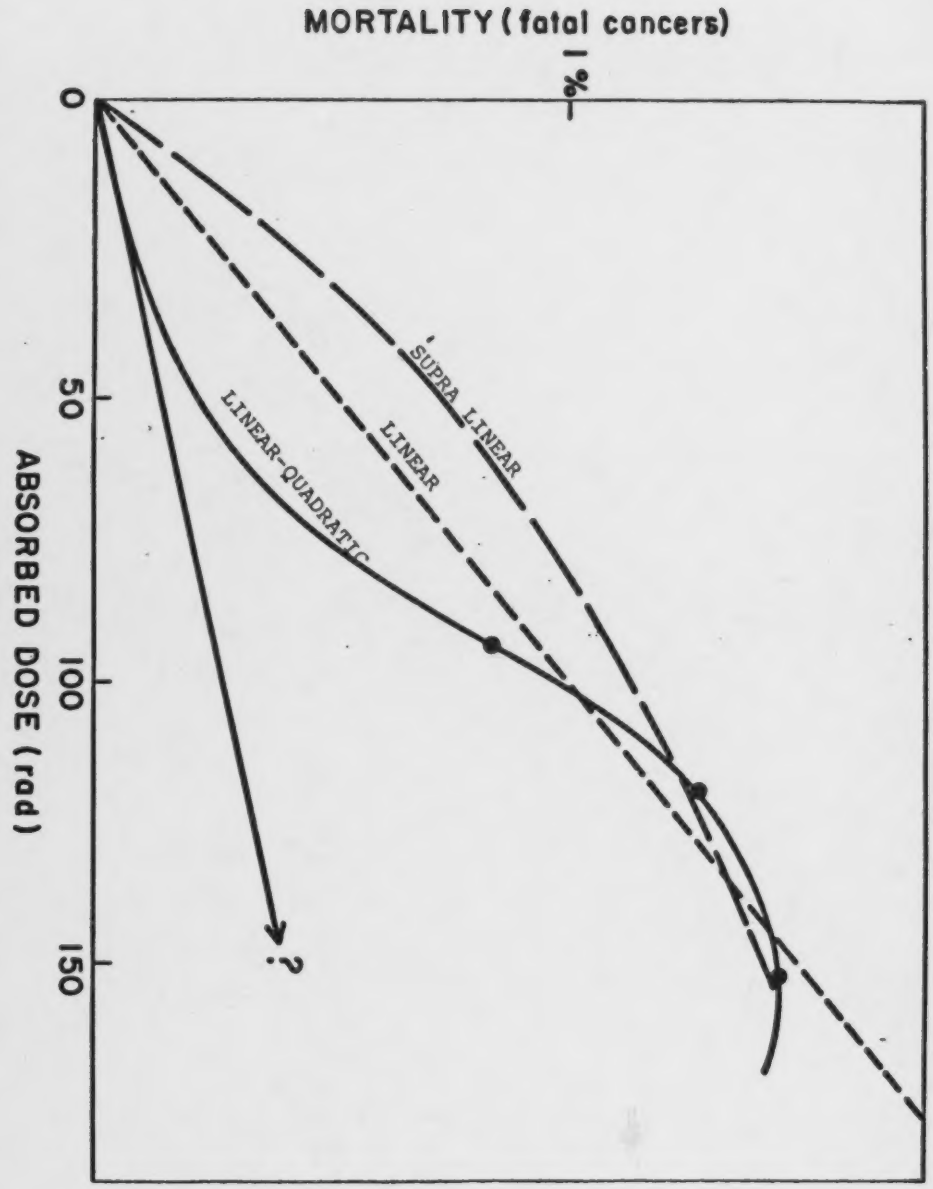
(1980)

	NO. OF WORKERS		MEAN EXPOSURE MREM		COLLECTIVE DOSE PERSON-REM
	TOTAL	EXPOSED	TOTAL	EXPOSED	
MEDICINE	477,500	218,600	70	150	32,600
INDUSTRY	371,800	196,700	120	230	46,200
NUCLEAR FUEL CYCLE	148,100	82,900	390	700	57,700
GOVERNMENT	178,600	56,300	60	200	11,100
MISCELLANEOUS	181,100	53,400	40	140	7,900
ALL WORKERS	1,357,100	612,900	110	250	155,500

EXPOSURE OF THE PUBLIC

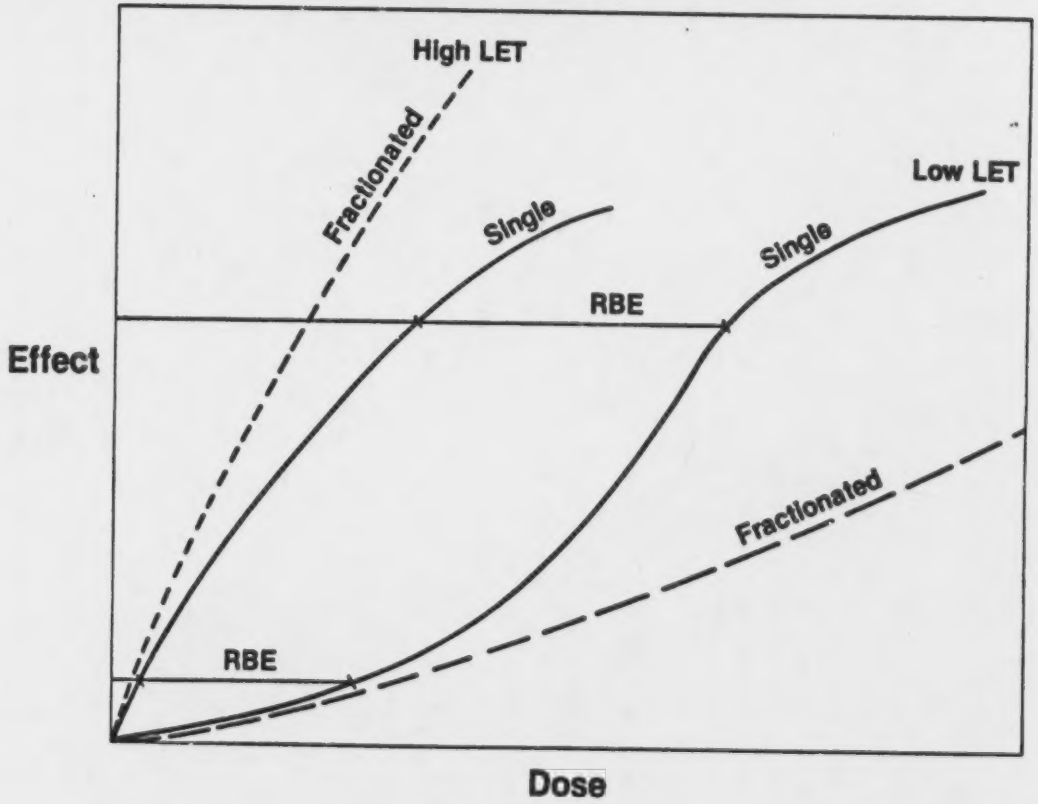
SOURCE	ANNUAL DOSE
Background Other than Radon (Terrestrial, Cosmic, Internal)	100 mrem
Radon - Average	200-350 mrem
Most Highly Exposed	2,000 mrem+
Medical Exposure	90 mrem
Occupational (Average)	250 mrem

Over a lifetime, these levels may be 5-10 rems or more.


MORTALITY (fatal cancers)
0
%
50
100
150
ABSORBED DOSE (rad)
SUPRA LINEAR
LINEAR
LINEAR-QUADRATIC
??

5

Dose Effect Relationships and RBE



Mrs. SCHNEIDER. Thank you.
Dr. Richmond, if you will.

STATEMENT OF DR. CHESTER R. RICHMOND, ASSOCIATE LABORATORY DIRECTOR FOR BIOMEDICAL AND ENVIRONMENTAL SCIENCES, OAK RIDGE NATIONAL LABORATORY, OAK RIDGE, TN

Dr. RICHMOND. Thank you. I'd like to give you several examples of some of the research accomplishments in the large biological and biomedical research program at Oak Ridge, and also try to show you how I think these programs are in jeopardy.

A couple of examples—I'll start with monoclonal antibodies, and I'll be very brief. Using monoclonal antibodies, the system is unique in that they, one, bind to a specific cell type of a tumor; they can be isolated in pure form in large quantities——

Mrs. SCHNEIDER. Excuse me. Before you proceed any further, please understand you're dealing with a novice. Exactly what are these antibodies, if you could give me a preliminary chemistry lesson here?

Dr. RICHMOND. I think that might come out as we get into this a little bit.

Mrs. SCHNEIDER. All right, very fine.

Dr. RICHMOND. Again, they're unique since these are chemicals that uniquely bind to a certain kind of cell, tumor cell; they can be isolated in large quantities, and they can be reproduced accurately from batch to batch.

We have been using this applied technology to attack experimental solid tumors in mice. For one type of cancer, a viral sarcoma—that's a cancer that grows in solid tissues—it doesn't have a comparable human analog. We have used monoclonal antibodies to attach to that particular cancer cell. They will not attach to the normal cells or other kinds of tumors. You might consider this to be analogous to using ZIP coding; these are very specific, they'll go to very precise locations through a chemical reaction of the antigen/antibodies.

We are very much interested in these because they have been used successfully in some types of human leukemias.

I'd like to jump to a whole different kind of research, back to where we started today, and that's on radionuclide generator development. And a brief example I'll give you is related to heart disease. These radio-nuclide generator systems are used as a convenient source of very short-lived daughter radio nuclides that are formed from a longer lived parent. We have developed a new, improved generator for an isotope called iridium-191 that has a half life of 5 seconds. This means it's very important in diagnosing heart ailments in children and adults. Since 1980 we've supplied this parent osmium radionuclide, which has a 15-day half life, to the Children's Hospital in Boston where the generators are prepared and separated iridium-191 is used to evaluate heart disease in children.

Advanced gamma imaging systems can take 12 to 15 pictures per second of the isotope as it is carried through the blood system of the patient. And any abnormal passages of blood between the heart

chambers can be easily detected and evaluated by this noninvasive technique. Some 20,000 children each year in the United States are born with a congenital heart defect that can be diagnosed in this way. Several pharmaceutical firms are interested in manufacturing the iridium generators because of the relatively long useful life, low cost, and ability to produce a radioisotope that has a short half life extremely short, extremely low-radiation dose to the patient, and a high yield of gamma rays that are easily detected.

Let me give you one more example, and this has to do with electron microscope tomography. Now, I know that sounds rather awesome to the nonspecialist, but you may have heard of the use of a concept on which this is based, called Computer Assisted Tomography, the so-called CAT scanners. The word actually comes from a Greek root that means to cut or look at a section. Basically, what we've done by combining groups of biologists and computer scientists at the laboratory is to develop a method to obtain quantitative, three-dimensional structural information from sections of biological materials. These are sections taken from electron microscopes, so they're extremely small in size. The technique does not involve a particular orientation of the materials under study, and we have been able to actually observe, through the reconstructed pictures that we get with the use of large computers, we can model the process of the actual transcription of the hereditary information during the synthesis of RNA, which is one of the important biological compounds, ribonucleic acid.

What's particularly interesting about this is that in a large multi-purpose laboratory, a lot of the activities such as this apply to different areas, and let me give you an example. This work is at the frontier of a number of fields: Electronmicroscopy, chromosome structure, and 3-D computer graphics. The implications extend considerably beyond the problems of immediate study. For example, in the field of cell biology, numerous organelles and large molecular structures can be studied. In this way we can help understand more of the mechanisms of cellular damage induced by chemicals or radiation. But this information can also be applied in areas as diverse as robotics, as well as the construction of microscopic objects. The impact of sophisticated imaging processes and display systems using advanced computers in this domain is just beginning to be felt, with vast consequences for a whole range of disciplines ranging from molecular biology to large-scale engineering development.

I think, in the interests of time, I'll not give any more examples but tell you why I think this program is in jeopardy. The proposed fiscal year 1985 budget for the programs at the Oak Ridge National Laboratory is about $2.5-million below the 1984 outlay. This deficit, about 14 percent, could result in the loss of as many as 35 people. For the past several years we have undergone similar large scale reductions in the total staff, and if one looks at a few more years of this kind of reduction in force, I believe we will be below critical mass in the sense that we cannot marshal large interdisciplinary teams to do large scale biological research.

I might mention that the utility costs are rising faster than related costs. In 1982, for example, it cost about $3 million, the utility costs, to run the large scale biological programs in terms of housing

for animals and the requirements for handling hazardous materials to protect the researchers. It's well known in the physical sciences that it costs money to run large accelerators and large physics machines, but it's not well realized or often realized that similar problems exist in maintaining the requirements, through electrical production and other utilities, to support large-scale biomedical research.

I might also mention that many committees have examined the laboratories in recent years and have made recommendations about multi-year support. And speaking as a research manager, I support this very strongly and it would sure help planning and managing research a great deal if we had fewer of the roller coaster-type fluctuations in the budgets from year to year.

During fiscal years 1981 to 1983 we lost 40 percent of the entire staff of our biology division. This resulted from decreases, not just from the Department of Energy programs, but also programs from other Federal agencies. And I think that if there is a message in my testimony, it is that our programs and others are at a critical point. Within a few years, if the funding patterns continue, they will no longer exist. They are about at a critical size in terms of supporting large scale research, at a time when OSTP and other parts of the Government are encouraging the involvement of the large laboratories to work with private enterprise and the universities, and there are many exciting ways that these kinds of activities could be pulled together. But again, I don't think enough people realize that some of these are in jeopardy and may not be here in a couple years.

Thank you.

[The prepared statement of Dr. Richmond follows:]

TESTIMONY PRESENTED TO THE

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH

AND ENVIRONMENT

OF THE

COMMITTEE ON SCIENCE AND TECHNOLOGY

U.S. HOUSE OF REPRESENTATIVES

MARCH 6, 1983

Good afternoon, Mr. Chairman and members of the subcommittee. My name is Chester R. Richmond. I am Associate Laboratory Director for Biomedical and Environmental Sciences at the Oak Ridge National Laboratory (ORNL) which is one of the major multipurpose scientific research and development institutions operated by various contractors for the U.S. Department of Energy. A biologist by training, I have practiced research for many years, and currently function as a research manager. As Director of a large Biomedical and Environmental Sciences program, I have had the opportunity to personally participate in the planning and implementation of health, safety, and environmental research related to both conventional and developing energy producing technologies. A major objective is to manage a multidisciplinary research program that will establish a sound foundation for estimating potential health impacts to man and his environment from various pollutants. A personal resume is included as Appendix A.

I am here at your request to discuss certain aspects of the Department of Energy's (DOE) Office of Health and Environmental Research (OHER) program. I am expressing my personal opinions. My objectives today are:

- to acquaint you with a small sample of the many research achievements arising from ORNL programs supported by DOE's OHER
- to show why these and related programs are national trusts that have continually responded to national needs and important societal issues
- to tell you why I believe these important programs are in jeopardy

Several of these objectives concern the scientific importance and uniqueness of the OHER research program. I will now discuss some of the more recent examples of ORNL research accomplishments. These range from analytical techniques involving atoms and molecules through subcellular and cellular level studies to those that use whole animals. The reason for such program diversity is given in Figure 1 which shows the interrelation among uncertainty, extrapolation, time and cost for the hierarchy of investigations ranging from structure-activity to epidemiological studies. The goal in many instances is to obtain information required for health effects assessments and, where possible, an identification of risk as related to exposure or dose. This information can then be used by decision makers and regulatory bodies as input to risk management activities.

My examples will deal with the lower end of Figure 1. My colleagues will deal with the upper end.

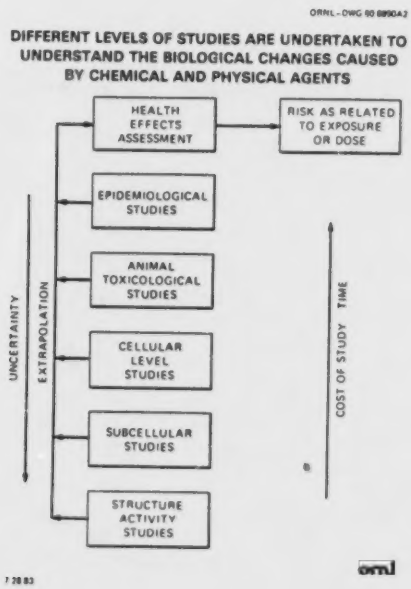


Figure 1. Hierarchy of Biological Studies

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MONOCLONAL ANTIBODIES

New biotechnology has been responsible for significant advances in understanding life processes at the molecular level and in applying this knowledge to problems such as cancer. One example is the ability to make monoclonal antibodies in what now must be regarded as rather routine fashion even if the advances that make it possible remain quite new and remarkable. Monoclonal antibodies are unique in that they (1) bind to a specific type of tumor cell (2) can be isolated in pure form in large quantities, and (3) are reproducible from batch to batch.

Biologists at ORNL have applied this technology to attack experimental solid tumors in mice. For one type of cancer, a viral sarcoma that does not have a human analog, a monoclonal antibody has been isolated that binds to that particular cancer cell but not to normal cells or other kinds of tumors. Scientists found that this antibody alone can destroy relatively large established tumors. From 20 to 30% of the test animals in a given group have been cured, with the cure rate depending on the antibody dose delivered and size of the tumor at time of treatment.

Studies of the mechanism of tumor destruction indicate that this antibody has a unique ability to interact with the host's lymphoid cells and that in concert, they eliminate the tumor cells. Such direct therapy using monoclonal antibodies already has been successful in the treatment of certain types of human leukemias.

In our own animal studies, we have also prepared monoclonal antibodies that react specifically with several mouse lung carcinomas. For reasons not yet understood, however, these antibodies lack the therapeutic effectiveness of the antibody to the sarcoma tumor. To circumvent this problem, we are attempting to use the specific binding properties of the antibody to deliver toxic agents or radioisotopes directly to tumor cells.

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This is analogous to the use of expanded zip coding to deliver mail to a specific location. One benefit of such specific targeting is that it reduces the relatively severe side effects of cancer chemotherapy.

RADIATION EFFECTS AND TRANSPOSABLE GENE ELEMENTS

Gene elements capable of transposition are known to be present as inherited genes in mammalian species, including man. These gene elements are important because they can cause genetic changes if they are stimulated to undergo transposition in the cell genome. One of these changes is the conversion of certain important cellular genes, called proto-oncogenes, into oncogenes leading to the formation of potential cancerous growth. In simple terms, "transposition" means that a gene element replicates itself, sends out its replicate copies, and "colonizes" by insertion into new locations in the chromosome while the parental copy still remains in the original location. The transposition event appears to be particularly responsive to environmental insults which cause DNA damages. It is well known that radiation causes DNA damages and, in the long run, may cause cancerous growth of the cells. Very little is known about the behavior of transposable gene elements in response to radiation.

Some recent findings are of interest. The RFM/UN mouse strain is considered an appropriate experimental model because these mice, like man, are susceptible to induction of myeloid leukemia by radiation. Our molecular analysis of the DNA of these radiation-induced leukemic cells has suggested that gene transposition events are associated with the leukemia induction. A particular retroviral gene, which is located on chromosome 5 and passed from parents to offspring of these mice like a normal gene, appears to have undergone "colonization" within the genome of radition-induced leukemic cells. In other words, in addition to the original single copy, additional copies of this retroviral gene are found to be in new DNA sites in these tumor cells. Recombinant DNA techniques have been applied to isolate the DNA clones of the original retroviral gene copy as well as those containing the "colonized" copies and new insertion sites. Because a specific oncogene is likely to be present at the new insertion sites of tumor

cells, the current studies are aimed at elucidation of the oncogene alterations as well as the chromosome translocation particularly associated with the radiation-induced leukemias in this experimental model.

ELECTRON MICROSCOPE TOMOGRAPHY (EMT)

The word "tomography" comes from a Greek root that means a cut or a section, as in an electron microscopy photograph of a thin layer of biological material. Through the collaboration of groups of biologists and computer scientists, a method has been developed to obtain quantitative three-dimensional (3-D) structural information from sections of biological materials. The technique is of general use because it does not involve a particular orientation or the internal symmetric properties of the materials under study. It is based on an extension of concepts employed in the computer assisted tomography (CAT) scanners (developed through OHER support) now so widely used in medical diagnosis.

Our goal is both to obtain 3-D structural information from sections of biological materials and then to use the reconstructed picture to model the process involved in the actual transcription of hereditary information during ribonucleic acid (RNA) synthesis. The processing sequence has six steps:

- Biological sections are photographed in a modern electron microscope equipped with a stage that tilts the specimen.
- The resulting micrographs are digitized by a scanning camera on line with an image processing system.
- The digitized images are aligned and registered about a common tilt axis.
- By using computer algorithms, a 3-D reconstruction of the biological space is developed.
- The reconstruction is displayed in 2- or 3-D sections.
- Models are built and spatial measurements are obtained by analysis of the computer reconstruction.

The biological problems of most immediate interest to us are concerned with the 3-D architecture of chromosomal regions engaging in key chromosomal transcription (i.e., the biosynthesis of RNA on chromosomal DNA in situ). We have studied the 3-D arrangement of nascent RNA around the central DNA axis, and the mode of folding of the nascent RNA by associated proteins. In addition, we have begun several projects employing a DNA specific stain for the electron microscope. Combined with EMT we should be able to trace and model in 3-D the path of DNA in situ in the transcribing gene. We are also examining by EMT the 3-D structure of inactive chromosome fibers and of regions engaged in DNA replication.

The work now in progress is at the frontier of a number of fields-electron microscopy, chromosome structure, and 3-D computer graphics. The implications extend considerably beyond the problems of immediate study. For example, in the field of cell biology, numerous organelles and supramolecular structures can be studied by this method, which could help us understand mechanisms of cellular damage induced by chemicals or radiation. In the field of computer graphics, in which ORNL has made pioneering use of digitized information from satellite imagery and ground-based sources for display and analysis of energy-related impacts, the result has been to combine computer hardware and software to quantitatively analyze 3-D images from several sources using electrons and light.

This information may be applied in areas as diverse as robotics and the reconstruction of microscopic objects. Previously, the world of 3-D has been difficult to analyze and visualize in a quantitative manner. The impact of sophisticated imaging processes and display systems in this domain is just beginning to be felt-with vast consequences for a whole range of disciplines from molecular biology to large-scale engineering development.

Time does not permit a detailed discussion of additional ORNL research accomplishments. I have included the following examples in Appendix B because they demonstrate the diversity as well as scientific excellence of the program.

1. The Importance of Anaerobic Bacteria (Infectious Disease and Energy Production)
2. The Carbon Dioxide Fixation Enzyme (Protein Engineering)
3. Radionuclide Generator Development (Heart Disease)

These are examples of fundamental and directed research. All three are research activities aimed at improving the quality of life.

At ORNL we are also interested in preventing detrimental health effects from energy producing technologies. I have included two examples of research accomplishments related to the production of liquids from coal. These, Reducing Bioeffects of Coal Liquids and Personnel Monitoring Technology are given in Appendix C.

GLOBAL ENVIRONMENTAL CONCERNS

Global Carbon Cycle

Your invitation letter asked me to cover ORNL research on the CO_2 problem. The following is a brief summary of that work and research on acid deposition.

ORNL's mission for the global carbon cycle program is two-fold. The first is scientific leadership in the development of global carbon simulation models and sensitivity and uncertainty analyses of key parameters as influenced by CO_2 emissions. Second is program management responsibility for DOE's entire research effort on modeling and most of the supporting field research. This effort involves four ORNL divisions as well as subcontracting and managing projects at nine universities and other federal laboratories. We hope to develop, by 1985, an overall assessment of the state of knowledge about the global carbon cycle. This assessment is designed to identify research necessary to develop an accurate prediction of future atmospheric carbon dioxide concentrations, which will assist DOE as the lead federal agency in establishing future research directions.

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In 1983, ORNL researchers produced the first high-resolution global map of major vegetation types ranked by their carbon storage capacity. The map will serve as a baseline to determine the effects of future forest clearing, reforestation, agricultural expansion, and desertification on the terrestrial absorption of CO_2. Large-scale mathematical simulations are being developed to predict the effects of increased warming on major agricultural and forested regions and the impacts of warming on the ability of sinks to retain carbon.

The goal of the ORNL-led efforts is to determine how much carbon is being ejected annually into the atmosphere in the form of CO_2. From an ecological and geochemical perspective this requires an understanding of the absorption capacities of "carbon sinks" such as the oceans and potential additional "sources" such as clearing of forests. Measurements taken at Mauna Loa Observatory in Hawaii since 1958 have shown a steadily increasing concentration of atmospheric CO_2. But that increase represents only about half of the carbon produced annually by human activities such as fossil fuel burning and forest clearing. The remainder is being removed and stored in the oceans and in part of the earth's vegetation. The objective, then, must be to determine the biological, chemical, and physical nature of the absorption processes on a global scale as well as factors that may limit or increase their ultimate capacity.

ORNL researchers have applied sensitivity and uncertainty analyses to investigate deviations in global carbon-cycle simulaton models from the Mauna Loa record. They found that the deviations are most sensitive to model inputs associated with the forest clearing record, the average depth distribution of carbon-14 in the ocean, the pre-industrial concentration of CO_2 in the atmosphere, and the temperature response of ocean surface waters to CO_2-induced climate change. The first of these represents the principal data which must be examined in attempting to resolve the role of the terrestrial biosphere. The last is important because it represents one facet of a potential climate feedback on the carbon cycle, namely the ocean's highly temperature-sensitive chemical equilibria which partially control the magnitude of air-sea exchange.

Acid Deposition

ORNL has a strong involvement in research on acid deposition to improve scientific understanding of the potential magnitude and mechanisms of environmental effects. We are investigating the ecological effects of acidification on streams, on forest nutrient cycles and agricultural crop productivity, and on forest growth in the Eastern U.S. We also continue to play a lead role in the National Laboratory Consortium which advises the Interagency Task Force on Acidic Deposition (created by the Acid Precipitation Act of 1980, P.L. 96-294) regarding national scientific priorities. The issues surrounding acidic deposition are complex and in some cases controversial. A lot of work remains to be done to assure that future research is focused in the right direction and that the results are interpreted scientifically and objectively.

As a DOE National Laboratory, we have at our disposal those resources and capabilities needed for high quality research, assessment, and data analysis.

We are very proud of these research accomplishments. If adequate support continues I believe we can make additional significant contributions, both practical and fundamental, that will reduce uncertainties associated with the health and environmental aspects of energy technologies. The real winners are the tax payers who, if past is prologue, will continue to reap the benefits traceable to research support provided by DOE's Office of Health & Environmental Research.

Appendix D lists recommendations made to DOE by its Energy Research Advisory Board (ERAB) concerning appropriate roles and missions for its laboratories. The DOE OHER supported programs have contributed significantly to most of these roles and missions.

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BIOTECHNOLOGY

I need to mention a concern I and others have about biotechnology. That is the possibility that the U.S. could lose its position of leadership in this important area to the Japanese. Today the U.S. is competing, at times unsuccessfully, in several areas of science and technology. For years the U.S. has had a virtually unchallenged lead role in biotechnology and other areas of the life sciences. Unfortunately, this situation may change and another currently strong U.S. activity may be compromised.

This problem has been addressed in a recent report by the Office of Technology Assessment (OTA) entitled "Commercial Biotechnology: An International Analysis". The report warns that our preeminence in leading the world in the commercialization of biotechnology may not continue. The report concludes that a well-developed life science base plus entrepreneurial spirit and the availability of financing for high-risk ventures have placed the U.S. in the position of leadership. However; if federal funding for basic life science research continues to decline, the science base, which is the underpinning of innovation in biotechnology and other activities, may be eroded.

I agree with this concern expressed in the OTA report. The OTA report was released by Rep. Albert Gore, Jr. (D-TN) who has said, "Biotechnology has, to date, been an American success story. A wise government investment has created a burgeoning and preeminent industry which creates jobs and helps our trade balance. It is imperative that we not let this advantage slip away from us, and we need to ensure that this industry is not crippled".

I believe biotechnology is an area in which the National Laboratories can make a major contribution to solving a national problem much as they have developed the science base of a strong U.S. nuclear

medicine commercial enterprise. Incidentally, we also are beginning to see more foreign competition in this area during recent years. Some radioisotopes are imported from the Soviet Union and South Africa. The National Laboratories can provide the interdisciplinary research and development teams needed for work in Biotechnology ... chemical engineers with experience in designing flow systems and bioreactors to house biological organisms or derivatives thereof, microbiologists, cell biologists, biochemists, molecular geneticists and specialists in growing cells in culture. These individuals can produce the science base that will feed private industrial organizations. The roles of private industry and the National Laboratories are complementary.

At ORNL we are in the process of establishing a "users facility" for Bioprocess Research. Both university and industrial researchers can work side-by-side with laboratory scientists in designated "users facilities". We hope to concentrate our work on tailoring enzyme systems to do what we want them to do. This tailoring is called by various names - protein engineering or site directed mutagenesis (techniques to genetically alter an enzyme which itself is a gene product).

The OTA report also concluded that federal funding of generic applied research and personnel training in areas of bioprocess engineering and microbiology may be insufficient to support rapid commercialization. The National Laboratories can contribute to the overall U.S. effort in these areas as well as the science base.

The DOE/OHER has recognized the importance of Biotechnology and has included activities in Bioprocess research into its long range planning. At ORNL we are reprogramming research efforts and using discretionary funding to add to ongoing work in bioprocess research.

IMPACT OF CURRENT BUDGET REQUEST ON ORNL RESEARCH PROGRAM

From FY 1982 to FY 1983 the DOE/OHER operating budget decreased by about 15% (budget authority-without accounting for inflation). The

comparable value for the ORNL portion of the DOE/OHER operating budget was a decrease of 14%. After adjusting the FY 1982 budget outlay by 6% for inflation the shortfall for ORNL programs in FY 1983 was $2.6 million or 9%.

If one uses a 6% escalation factor (increase costs of doing research), then the FY 1982 to FY 1983 decrease at ORNL was equivalent to about 18.5%. This resulted in the loss of 42 people, mostly in biology. This followed smaller reductions between FY 1981 and FY 1982.

Currently we are facing a shortfall for FY 1984 that will be less severe than that for FY 1982 to FY 1983.

The proposed FY 1985 budget for ORNL is $2.5 million below the estimated FY 1984 budget outlay. This deficit, about 14%, could result in the loss of as many as 35 people.

During FY 1981-83 we lost 40% of all ORNL Biology Division employees. This loss resulted from decreases in support from DOE/OHER and other federal agencies. Much time and effort was spent on activities associated with reductions in force and reassignment of remaining personnel. Other divisions were impacted but less severely. I fear we, and other OHER supported labs, may be approaching the point where we will be below the "critical mass" required to conduct large multidisciplinary research projects. Such losses would be tragic.

Recently, three committees were, established as part of the Administration's efforts to review DOE programs. They were:

- The President's Private Sector Survey on Cost Control (Grace Committee)
- The multiprogram Laboratory Panel of the Energy Research Advisory Board (ERAB)
- The Federal Laboratory Review Panel (Packard Committee) established by the White House Science Council (WHSC)

Each committee voted that both direction and performance of federal laboratories is negatively impacted because of the instability of support.

The Grace Committee recommended three year rolling budgets and The Packard committee recommended multi-year funding authorizations for the laboratories. The ERAB panel called for two year rolling appropriations. I fully support the concept of multi-year funding which would provide more stability and allow for better research planning and management.

Utility costs are rising faster than other research related costs. In FY 1982, for example, utility costs associated with our biological work were $3 million. These costs result from stringent requirements for working with toxic material and maintaining large numbers of animals for research. Some of the large cost is related to the buildings that were built decades ago and are energy inefficient. We are working to reduce this cost component. We have closed several small buildings and portions of the main biological research building during the past year to reduce utility costs. These disruptive actions also added additional costs.

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SUMMARY

In summary, I would leave the following messages with you. The DOE/OHER programs fill an important niche and contribute significantly to the solution of real world problems and to the nations knowledge base. However, this program is in jeopardy and may be irreparably damaged via attrition during the coming years.

During the past several years people have asked, "when will the precipitous decrease in funding for the DOE/OHER programs stop?" Now they ask, "Will there be a viable OHER program in DOE by 1990." Many of our outstanding scientists and managers may not wait to see what happens.

APPENDIX A

CURRICULUM VITAE

Name: **CHESTER ROBERT RICHMOND**
108 Westwind Drive
Oak Ridge, Tennessee 37830

Telephones: Business: (615) 574-4333; FTS 624-4333
Home: (615) 483-8826

Birth Date: May 29, 1929

Employer: Union Carbide Corporation Nuclear Division

Where Employed: Oak Ridge National Laboratory
P. O. Box X
Oak Ridge, Tennessee 37830

Positions: Associate Laboratory Director for Biomedical and Environmental Sciences (1974-present)
Director of Health, Safety, and Environmental Affairs for Union Carbide Corporation's Nuclear Division (1981-present)

Education: B.A. Biology, New Jersey State College, Montclair (1952)
M.S. Biology, University of New Mexico, Albuquerque (1954)
Ph.D. Biology-Physiology, University of New Mexico (1958)

Major Research Interests: Radiobiology, Radiation Effects, Health and Environmental Effects of Energy Production

Experience: Student-trainee, Biomedical Research Group, Los Alamos Scientific Laboratory, University of California, Los Alamos, New Mexico (1955-58)
Staff Member, Biomedical Research Group, Los Alamos Scientific Laboratory, University of California, Los Alamos, New Mexico (1958-62)
Section Leader, Mammalian Metabolism, Los Alamos Scientific Laboratory, University of California, Los Alamos, New Mexico (1962-68)
Medical Research Branch, Division of Biology and Medicine, U.S. Atomic Energy Commission (now Office of Health and Environmental Research, Department of Energy), Washington, D.C. (1968-71)
Group Leader, Biomedical Research, Los Alamos Scientific Laboratory, University of California, Los Alamos, New Mexico (1971-73)
Alternate Health Division Leader, Los Alamos Scientific Laboratory, University of California, Los Alamos, New Mexico (1973-74)

Associate Laboratory Director for Biomedical and Environmental Sciences, Oak Ridge National Laboratory, Oak Ridge, Tennessee (1974-present)
Professor, The University of Tennessee-Oak Ridge Graduate School of Biomedical Sciences, Oak Ridge, Tennessee (1975-present)

Professional Societies:

New York Academy of Sciences, 1952-1960
Kappa Delta Pi, 1950-1952
Phi Sigma, 1954-1958
Sigma Xi, May 14, 1957-present
Radiation Research Society, 1963-present
American Association for the Advancement of Science, 1965-present
Fellow, December 20, 1966
International Radiation Protection Association, Charter Member, 1966-present
Health Physics Society, Charter Member, 1957-present
Society for Experimental Biology and Medicine, 1962-1977
American Association for Public Health, July 1977-1980
Society for Risk Analysis, Charter Member, 1980-present

Committees, Panels, Special Assignments Partial List

Atomic Energy Commission/Division of Biology and Medicine Committee on Space Nuclear Radiological Safety Matters (1968-73)
Member, Ad Hoc Plutonium Committee of the Nevada Applied Ecology Group (1970-1972)
Chairman, Plutonium Committee of the Nevada Applied Ecology Group (1972-1976)
Advisory Committee for the Center for Human Radiobiology, Division of Radiological and Environmental Research, Argonne National Laboratory (1972-76)
Transuranium Technical Group, U.S. Energy Research and Development Administration - American Institute of Biological Sciences (1972-76)
Enewetak Atoll Radiological Status Group. Advisory to US DOE Radiological Assessmen Review Group (1972-1973)
Medical Isotope Advisory Committee, State of New Mexico Environmental Improvement Agency (1974)
East Tennessee Cancer Research Center, Executive Council (1974-77)
ORNL representative for Association of American Cancer Institutes (1974-present)
Executive Committee, Oak Ridge National Laboratory (1974-present)
Senior Planning Group, Oak Ridge National Laboratory (1974-present)
Consultant, Advisory Committee on Reactor Safeguards, Nuclear Regulatory Commission (1975-80)
National Council on Radiation Protection and Measurements:
Council Member (1975-)
Scientific Committee No. 30, Physical and Biological Properties of Radionuclides (1969-1979)
Scientific Committee No. 31, Selected Occupational Problems Arising From Internal Emitters (1969-1979)

Consultant to Scientific Committee 57 (1981-present)
Ad Hoc Committee on Potential New NCRP Publications (1982)
Member, Energy Research and Development Administration Technical Information Panel (1976-77)
Enewetak Atoll Cleanup Advisory Group. Advisory to US DOE (1977-1980)
Member, Energy Research and Development Inexhaustible Energy Resources Study — Environmental Panel (1977-78)
International Commission on Radiological Protection, Committee 2 (1977-)
National Academy of Sciences/National Research Council Planning Conference on Synthetic Fuels, October 1979
Steering Group for the Society for Risk Analysis (1979-1980)
Southeastern Regional Coordinator for DOE Earth Day Activities, 1980
Energy Health Science Review Panel for Environmental Protection Agency (1980-1981)
Member, Department of Energy, Energy Research Advisory Board, Panel on Light-Water Reactor Research and Development Reactor Safety Research and Development (1982-present)

Honors & Awards:

USAEC Special Achievement Certificate, May 1970
Certificate of Meritorious Service, University of Utah, October 1970
E. O. Lawrence Award, June 1974
USAEC Certificate of Appreciation, 1975
G. Failla Lecture and Award, Radiation Research Society, 1976

Citations:

Biographical Directory of the American Public Health Association
American Nuclear Society's Communicators Directory
American Men and Women of Science
Men of Achievement

Skills:

Familiar with whole-body radiation detectors and some radiation equipment used in field; general familiarity with field of animal and human radiobiology including both early and late effects from radiation; major emphasis on internal emitters in animals and man from the viewpoint of metabolic kinetics and biological effects; research management.

Avocations:

Comparative Risk, History of Science, General Biological Science

February 1984

APPENDIX B

RADIONUCLIDE GENERATOR DEVELOPMENT (Heart Disease)

Radionuclide generator systems are used as a convenient source of very short-lived "daughter" radionuclides that are formed by the radioactive decay of a longer-lived "parent." ORNL has developed a new, improved generator for the radioisotope Iridium-191m with a half-life of 5 seconds which has become very important in diagnosing heart ailments in both children and adults.

Since 1980, ORNL has supplied the parent osmium-191 radionuclide, with a 15-day half life, to Children's Hospital in Boston where the generators are prepared and the separated Iridium-191m is used to evaluate heart disease in children. Advanced gamma-camera imaging systems can take 12 to 15 pictures per second of the radioisotope as it is carried along in the patient's bloodstream. Abnormal passage of blood between the heart chambers can be easily detected and evaluated by this non-invasive technique, and patients identified for surgery. Iridium-191m is particularly well-suited for pediatric use because its ultra-short half-life results in a very low radiation exposure and clearing within minutes for repeat studies. Some 20,000 children each year in the U.S. are born with the congenital heart defect that can be diagnosed in this way.

Several pharmaceutical firms are interested in manufacturing iridium generators because of their relatively long useful life, low cost and ability to produce a radioisotope with optimal properties--extremely short half-life, extremely low radiation dose to patients, and a high yield of gamma photons at an energy level that is efficiently detected.

THE IMPORTANCE OF ANAEROBIC BACTERIA (Infectious Disease and Energy Technology)

During the past few years researchers at ORNL have investigated the phenomenon of anaerobes, a group of bacteria that cannot survive in the presence of even small amounts of molecular oxygen. To fully appreciate the role of anaerobes in the natural environment and to enable scientists to apply sophisticated techniques such as gene splicing and other genetic manipulations to them, we must first grow them conveniently and readily in the laboratory.

Our current work on the growth of anaerobes is based on earlier basic radiation microbiology studies initiated at ORNL in the sixties. Our studies concerning the ability of the membrane fraction to stimulate division in irradiated cells and remove oxygen involved many quantitative determinations. We concluded that the membranes removed oxygen because they contained a system of enzymes which transferred hydrogen atoms from various medium components to oxygen, thereby producing water. Subsequently, we considered the possibility that membrane fragments might be a valuable way of removing oxygen from bacteriological media designed to support the growth of anaerobes. Over the past two years, we have used the membranes to grow 18 different species of anaerobic bateria representing 8 different genera. We have conducted experiments using both liquid and solid media. All organisms

tested have grown well in the presence of the membrane fraction; indeed, some of them have grown much better than in conventional anaerobic media.

One implication of these tests is the possibility of early and sensitive detection of certain diseases. For example, members of the genera Bacteroides and Peptostreptococcus, which are involved in infections of soft tissues in humans and animals, grow rapidly and luxuriantly in membrane-containing liquid media. Thus, their presence in a clinical specimen could be detected earlier and more reliably than by the use of currently available techniques.

In planning for advanced methodologies in biotechnology, a field in which anaerobic bacteria figure prominently, the use of membrane fractions to remove oxygen appears to have several advantageous features that make it a preferred alternative to currently available methods.

We expect that our new techniques will allow us to perform more sophisticated experiments with anaerobes in fields where they are used to manufacture chemicals such as fuels, solvents, and chemical intermediates. Many genetic manipulation techniques developed for oxygen-tolerant species through radiobiological research may become applicable to anaerobic organisms in biotechnology. .

THE CARBON DIOXIDE FIXATION ENZYME (Protein Engineering)

Because biomass is a renewable energy source, there is special interest in an enzyme that plays a vital role in plant productivity. This enzyme ribulosebisphosphate carboxylase, or simply the CO_2-fixation enzyme, catalyzes the photosynthetic conversion of atmospheric carbon dioxide into carbohydrates—100 billion tons annually on a global basis, produced by ten million tons of the enzyme itself. But atmospheric oxygen, as a substrate and inhibitor of this same enzyme, interferes with the process. Hence plant growth is found to be more rapid under low oxygen tension. The effect of this dual role of the CO_2-fixation enzyme can be to cut plant yields in half.

During the past year, ORNL researchers have made substantial progress in elucidating certain structural features of the CO_2-fixation enzyme that ultimately might provide a basis for diminishing the undesirable effects of oxygen. Because it is impractical under field conditions to decrease the oxygen level in the atmosphere, the strategy is to modify the enzyme in a beneficial way so that oxygen is no longer inhibiting.

Sophisticated protein-modifying agents called affinity labels have permitted identification, location, and schematic representation of the enzyme's constituent amino acids at the catalytic or reactant site. Also, comparative sequence studies of evolutionarily diverse species of the CO_2-fixation enzyme have confirmed the structural invariance of these catalytic site regions. Now that the catalytic site has been partially characterized, methods of genetic engineering can be applied to generate mutant forms of the enzyme in which these amino acids are replaced by different ones.

The long-term goal is to dramatically improve plant yields for food and biomass production. Being able to characterize structural and mechanistic features of the enzyme provides the experimental basis for systematically altering the chemical environment at the catalytic site to diminish the effects of oxygen. If this can be achieved in plants, greatly increased yields will ensue.

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APPENDIX C

REDUCING BIOEFFECTS OF COAL LIQUIDS

The potential environmental and health effects including cancer of crude, coal-derived synthetic fuels are considered to be more severe than those of petroleum crudes. Investigating treatment processes that promise to reduce the bioeffects of coal liquids has been a task of a cooperative Fossil Energy/Life Sciences Synthetic Fuels Programs study involving an interdisciplinary team of scientists. Researchers have been studying the effects of hydrotreatment, a process used in petroleum refining in which oil is heated under hydrogen pressure in the presence of a catalyst. Blends of middle and heavy distillates from three coal-liquefaction processes have been water washed and subjected to different levels of hydrotreatment. ORNL's role has been to characterize the chemistry and bioactivities of the treated samples.

Our results show that regular changes in the properties of the sample occur with increasing levels of hydrotreatment: the sample becomes more volatile, less dense, and less viscous. Its heteroatomic content (sulfur, nitrogen, and oxygen) as well as the presence of potentially carcinogenic polycyclic aromatic hydrocarbon (PAH) compounds in it decrease as hydrogen is incorporated into it. These gross changes are reflected in more detailed measurements.

For example, the weight percentages of both the ether-soluble acid and ether-soluble base fractions as well as the PAH fraction decline by factors of 10 to 20. Phenol, a toxic component, drops even more precipitously, as does the carcinogen benzo[a]pyrene. Similar decreases are noted for mutagenic, nitrogen-containing aromatics. These data are supported by the results of multiple bioassays, which indicate that the biological activity of the sample decreases with an increase in the severity of hydrotreatment. On the other hand, washing the product in water before hydrotreatment does not decrease its biological activity. Our conclusion, therefore, is that hydrotreatment is a very useful refinery process for upgrading coal liquids.

We are exploring additional ways of reducing bioactivity. Our findings so far indicate that methods such as acid washing, thermal distillation, solvent extraction, and charcoal or power plant hopper-ash adsorption are potentially promising in removing mutagens. Whether these methods also can remove other types of hazardous compounds-toxicants, teratogens, or carcinogens-from synfuels products remains to be investigated.

PERSONNEL MONITORING TECHNOLOGY

Among the potential health hazards of coal-liquefaction processes is a class of suspected carcinogens known as polycyclic aromatic hydrocarbons (PAH). The PAHs, which cause cancer in experimental animals, are common in coal tars.

One new approach to personnel monitoring has been to detect possible human physiological response to PAH exposure, as measured by a sensitive and specific biochemical indicator. This work has been carried out by a team of chemical engineers, biologists, biochemists, physicists and electrical engineers. PAHs are metabolized in people by the mixed-function oxidase (MFO) enzyme system. Because the carcinogenic potential of reactive PAHs can be either diminished or enhanced by the metabolic activity of the MFO system, the amount of MFO activity induced by a PAH is considered an indicator of the toxicity of the PAH. The MFO activity is determined kinetically by measuring the rate of formation of a highly fluorescent material, resorufin, produced by the oxidation of the 7-ethoxyresorufin substrate.

So far, these tests have demonstrated a dose-response relationship between the MFO activity and the exposure of test animals to various materials, including coal liquids. In a study of a series of natural and synthetic petroleums, the magnitude of induction of MFO activity of each test material corresponded to its previous ranking as a carcinogen and mutagen. In other words, a coal liquid ranked as highly potent in causing cancer and genetic mutations in animals was found to induce also a large amount of MFO activity.

Although measurements to date have been limited to samples from mouse-liver microsome, they are to be extended to human body fluids and skin. Because of the decreased amount of the MFO enzyme system present in the body samples, an argon laser has been interfaced to a centrifugal analyzer, thus making the fluorometric measuring system at least 100 times more sensitive. With this gain, it is expected that the system will be able to monitor, from whole blood samples, the physiologic response of plant personnel to potential carcinogenic or mutagenic compounds that may arise in the synthetic fuels industry.

APPENDIX D

ENERGY RESEARCH ADVISORY BOARD (ERAB) LAB STUDY RECOMMENDATIONS

THE APPROPRIATE ROLES AND MISSIONS OF THE LABORATORY

VIS-A-VIS UNIVERSITIES AND INDUSTRY

ERAB RECOMMENDATIONS

- Perform Department's "national trust" mission in fundamental research in the physical sciences, including high energy and nuclear physics and radiobiological sciences (including nuclear medicine). Sustain scientific staff capabilities and research facilities for laboratory research and for use by other Federal agencies and the private sector.
- Perform research and development on the health, safety and environmental externalities incident to promising energy technologies.
- Perform generic research and development where judged to be in the public interest or where, for economic or technical reasons, industry does not choose to support it.
- Act as agents for the Department in exercising broad technical management responsibilities, including multilaboratory and/or subcontracted R&D.
- Make special capabilities and expertise available to other Federal agencies, State and local governments, universities.
- Contribute to education and training of scientists and engineers.

Mrs. SCHNEIDER. Very fine. I thank all of you for your testimony. I have a whole slew of questions. I'd like to begin with Dr. Sinclair. In your testimony you made several references to the studies that are going on with the Japanese and their exposure to the Hiroshima bomb. I'm wondering about some testing that may be going on with U.S. soldiers, who are now referred to as "Atomic Veterans" who were exposed during the testing phases and who continued to be exposed during the testing phases of atomic bombs?

Dr. SINCLAIR. I wouldn't know about continuation, Mrs. Schneider. I do know that some of the soldiers who were exposed in the earlier tests in Nevada are being investigated, of course, in a program through the National Academy of Sciences.

Mrs. SCHNEIDER. You had also mentioned—just let me make note of that—that we don't really have much information about the genetic effects about the impact of plutonium, and then third on therapy, the impact on therapy and also occupational exposure. I'm just curious, and I have to put this in a more simplistic point of view, of course, but having myself had radiation therapy, for example, the doctor had told me that if I had additional exposures the cumulative amount of radiation could cause some other form of cancer. Now I'm just wondering, also serving on the Energy Subcommittee, there are discussions of exposure of workers who are working with light water nuclear reactors. Now, I recall also that there were commercials run by the nuclear industry some time ago that said that you will receive more radiation exposure if you are standing on the steps of the Capitol—which I often do—or flying in an airplane, which I do every weekend to my constituents, and a whole broad spectrum of other examples. Now, I am curious as to what kind of research—and if you want to use a personal example of myself, that's fine, because I have had radiation therapy, I fly in airplanes, I stand on the steps of the Capitol, and who knows, God forbid, what other kinds of exposures that I am currently being subjected to—what does that all mean? What kind of research have you people put together?

Dr. SINCLAIR. Well, in responding, the point of my testimony was to say that in certain instances we have direct human information; the Japanese are a good example.

Mrs. SCHNEIDER. Right.

Dr. SINCLAIR. I might list also a number of others that would interest you because they deal with pelvic radiotherapy, for example, groups of women who were treated years ago and now have a greater incidence of various different tumors. That is a consequence, and it could be a consequence in your own case. The risk may not be very high; it depends on the dose and the circumstances, but in order to be treated, in order to be cured of the one disease, you may run the risk of another. And they do provide us with very definite information about what dose levels cause the injurious cancers. But again, my point was that all of that information is at relatively high doses. If you receive radiation treatment for Hodgkin's it is at fairly high doses. We as human beings expect, in the nuclear power industry and hopefully everywhere else where we do things deliberately, to avoid high doses altogether, except for therapy, and to be exposed only to low doses. And that's why we're so interested, and why we find it so difficult to predict

the effects of low doses because the information is in high doses; we want to get down to the low doses, and there isn't a simple relationship between them. We try to get that from the laboratory. From animal systems, plant systems, and so on. And we have been pushing the dose information downwards steadily with time because you have to start somewhere.

And I mentioned the genetic effects and the plutonium and high-LET radiation in neutrons because those are three examples where we have either very scant given information or none at all, and where we have to go to a laboratory not just to support the extrapolation from the high doses to the low doses, but to get everything we know about them. And by and large that's true, in the case of neutrons.

Mrs. SCHNEIDER. Well, if one says don't worry about the low doses, shouldn't one worry about the cumulative impact of those low doses?

Dr. SINCLAIR. Yes, indeed. It's a matter of—to come back to the comparison that I think you referred to, that the nuclear power people make, there is one of my viewgraphs—this one—which gives some of the sources to which people are exposed each year. And it tells you, for example, natural background sources—other than radon—about 100 millirems. Radon sources, probably about 200 to 350 millirems, indoor radon being one of our important public problems. Occupational exposures on the average being about 250 millirems for those who are occupationally exposed, and that, I am sure, is why the nuclear power people were making the comparison. In general, their occupational exposures are not that much higher than some of the others that we're exposed to elsewhere. But the cumulative effects of all of them, of course, would make you a good subject for study if you'd had more than most, for example. Our principal limitation is that we don't have enough people exposed at enough levels for us to be able to judge in that population as compared with another that has not had that exposure, exactly how many chances there have been except in very specific cases like the Japanese.

Mrs. SCHNEIDER. Well, that leads me to another question. In some of your radiation protection and measurement studies, is most of your research being conducted on rats or on human beings?

Dr. SINCLAIR. We depend on the laboratories of these gentlemen here, my former laboratory, the Argonne National Laboratory, and the university programs, to provide the assessments that result in our reports. And those experiments are done in a wide variety of animal systems, the most important general one being the mouse. But his older brother if you like, longer-lived brother, the dog, is very important as a staging animal in life span between the mouse and man. And we've found a number of generalizations about life span that enable us to extrapolate some of the information we have in the mouse, via the dog, to man.

Mrs. SCHNEIDER. There are various arguments often put forward about why we should not change the radiation protection levels or lower the radiation protection levels. Some have said, well, we don't want to alarm the general public, which is certainly an argument that I don't buy, but then there's an economic argument. And last year Dr. Grasmere had indicated it would cost approximately

$3 billion if radiation protection levels had to be lowered. Do you have similar numbers that indicate that there would be this kind of economic impact if we provide adequate radiation protection?

Dr. SINCLAIR. Well, I have no reason to disbelieve some of the numbers that are given economically, but our Council would not be making recommendations based on the economics of the situation in general but rather on advice with respect to protection measures. And it's because the average in this occupational case is down close to the region where the public gets exposed from background sources and medical and so on, too, that at the present time many consider the occupational levels reasonably satisfactory because they lead to that average.

Mrs. SCHNEIDER. All right.

Dr. SINCLAIR. Not perfect, by the way, just reasonably satisfactory.

Mrs. SCHNEIDER. All right. Could some programs that are similar to those which DOE is currently sponsoring be conducted at some of the universities around the country rather than at the national labs?

Dr. SINCLAIR. Well, in dealing with——

Mrs. SCHNEIDER. Any of you that would like to answer that are welcome to.

Dr. SINCLAIR. Do you mind if I say something, and then I'll let them have a turn?

Mrs. SCHNEIDER. Sure.

Dr. SINCLAIR. It's a question that I think we've wrestled with in the national labs at many times, and the labs were set up to have special facilities and to have special accumulations of people, and especially to do long term things. They have probably done most things because of the way in which they were organized better than a university could have done it, just because of the permanence of the facilities, the people, and the structure. But many other things, I think we'd agree, could be better done or as well done in universities.

Mrs. SCHNEIDER. OK.

Dr. Richmond?

Dr. RICHMOND. I'll try also, thank you.

I happen to have with me some information on the Office of Health and Environmental Research budget for fiscal year 1983, and it turns out that about half, approximately, of the total funding goes to the larger national-type laboratories. The remaining is allocated to universities and other research-kind of organizations. The reason I think that it makes sense to have a portion of the total budget in the national laboratories is that we have large facilities that are not available in other areas. Let me give you one example, since we've been touching on nuclear medicine quite a bit today.

You need large reactors or calutrons, different machines that can produce either the stable isotope, which can be used in some kinds of activities or research, or a radioactive form that is sometimes made from a stable element. So you need the large physical facilities. You need hot cells, you need the interdisciplinary teams, the chemists who can take that particular radioactive element and build it in a chemical compound. And at that stage, very often,

these materials are handed off to private enterprise, to commercial enterprises and private business. We don't get involved in that end of the business. We have cooperative programs with hospitals throughout the United States. But very often you don't have that combination of resources in a university, for example, to be able to do that kind of thing. It's just one example.

Dr. BOND. I can't add very much to that, but I would like to reaffirm what's been said, that the national laboratories do have the special facilities for irradiation, for instance, that would not be easily manned and operated at universities. And some are very expensive and highly unique; for instance, some kinds of radiobiological work can be done only on a machine like the Bevalac at Berkeley. It wouldn't make sense to try to duplicate that at universities.

The last point I would like to make is that the facilities for housing and looking after the animals are very special and they are very costly. These have been established at the national laboratories. For this work now to be done elsewhere, in universities, would require building similar laboratories at a great cost. It just doesn't make any sense to me to relocate that kind of study.

Mrs. SCHNEIDER. OK, thank you.

Dr. Richmond.

Dr. RICHMOND. That reminds me of an excellent example that Dr. Bond touched on, the mammalian genetics studies. And of course you can study genetics at the chromosomal level or the molecular level, but there are only basically two large facilities in the entire country to study mammalian genetics. One is the Jackson Laboratory in Bar Harbor, ME, and one is at Oak Ridge. So that's where the facilities are; that's where they exist. And it would be a large investment of money to try to duplicate these afresh somewhere.

Mrs. SCHNEIDER. One of you had mentioned indoor radon in your testimony. Is that you, Dr. Sinclair?

Dr. SINCLAIR. Yes.

Mrs. SCHNEIDER. Well, whether you are aware of it or not, there had been an effort to have research conducted on indoor air pollution and unfortunately that was removed from the budget. And yours truly is spearheading that effort to reintroduce funding for indoor air pollution. But let me also ask, if there are no other points—are there any other points that any of the three of you would like to make? We'll call this hearing to a close. If not—any other comments, questions, or remarks?

[No response.]

I will say that I feel responsible to apologize for the lack of attendance by my colleagues at this hearing because I find the topic to be critically important. I do not know the reason why they aren't here, but I do think that it would be useful for each of you to convey your message, perhaps in writing, to the members of this committee because this budget line item will come up as a topic of discussion and debate and the fact that they were not able to be here to hear your testimony, I think, might lead them to support the budget that has been proposed. I personally have some thoughts, and perhaps even some plans, to introduce an alternative budget for your purposes, and I will be thinking and working on that as soon as I have a breather, which will probably be next

week. But I cannot push forward such proposals for increased spending or a shift in spending priorities unless I have additional support. And obviously, not having any other members here, I may need some help from all of you.

I thank you for your testimony and your patience and look forward to hearing from you in the near future.

I now conclude this hearing. Thank you.

[Whereupon, at 4:00 p.m., the committee recessed, to reconvene at the call of the Chair.]

CANCER AND OTHER HUMAN DISEASES: DOE RESEARCH PROGRAMS

TUESDAY, MARCH 13, 1984

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE
RESEARCH AND ENVIRONMENT,
Washington, DC.

The subcommittee met, pursuant to notice, at 2:10 p.m., in room 2318, Rayburn House Office Building, Hon. James Scheuer (chairman of the subcommittee) presiding.

Mr. SCHEUER. The hearing of the Subcommittee on Natural Resources, Agriculture Research and Environment of the Science and Technology Committee will come to order.

Today, as you know, we are going to hear from Dr. Alvin Trivelpiece, Director of the Office of Energy Research of the Department of Energy.

I have a statement which I would like to place in the record. There beimg no objection, so ordered.

[The opening statement of Mr. Scheuer follows:]

OPENING STATEMENT OF
JAMES H. SCHEUER
MARCH 6, 1984

THE SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT WILL COME TO ORDER.

ONE OF THE MAJOR HEALTH PROBLEMS FACING AMERICA IS CANCER WHICH RESULTS IN THE DEATH OF OVER 400,000 AMERICANS EACH YEAR.

THE DEPARTMENT OF ENERGY (DOE) HAS A MAJOR RESEARCH EFFORT UNDERWAY TO DETERMINE WHETHER EXPOSURE OF HUMANS TO RADIATION AND CHEMICALS ASSOCIATED WITH ENERGY PRODUCTION AND USE RESULTS IN CANCER.

OTHER DOE RESEARCH EFFORTS
FOCUS ON THE USE
OF RADIATION TO
TREAT CANCER.

SINCE CANCER OFTEN DOES
NOT MANIFEST ITSELF
UNTIL YEARS AFTER
EXPOSURE, LONG-TERM
STUDY IS NEEDED.

IN ORDER TO CONDUCT THE
NECESSARY RESEARCH,
A COMMITMENT TO THE
NECESSARY LONG-TERM
FUNDING BY THE
ADMINISTRATION IS
ALSO MANDATORY.

PAST ADMINISTRATIONS HAVE COMMITED THEMSELVES TO THE SUPPORT OF THE EXCELLENT CANCER RESEARCH PROGRAMS WITHIN THE DEPARTMENT OF ENERGY.

HOWEVER, DESPITE THE IMPORTANCE OF UNDERSTANDING THE CAUSES OF CANCER, WHICH CAN LEAD TO CURES, FUNDING FOR THIS RESEARCH HAS INCREASED ONLY SLIGHTLY IN THE FY 1985 BUDGET REQUEST (FY 1985 $52.4 MILLION, FY 1984 $51.3 MILLION), WHICH IS LESS THAN A COST OF LIVING INCREASE.

THEREFORE, THIS MODEST INCREASE IS NOT SUFFICIENT.

IN FACT, ONE OF THE NATION'S OUTSTANDING CANCER RESEARCH LABS AT THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, (UCLA) IS SCHEDULED TO BE TERMINATED AND WILL RECEIVE NO DOE FUNDS IN FY 1985.

TODAY'S WITNESSES, INCLUDING REPRESENTATIVES FROM UCLA, WILL EXPLAIN SPECIFICALLY HOW THE FY 1985 BUDGET WILL IMPACT ON THE CANCER RESEARCH PROGRAM.

WHILE I APPLAUD EFFORTS TO REDUCE UNNECESSARY AND DUPLICATIVE EFFORTS, MANY OF THE PROPOSED BUDGET CUTS APPEAR TO BE ARBITRARY, EXCESSIVE, AND WITHOUT MERIT.

THE AMERICAN PEOPLE DESERVE TO KNOW WHAT THESE CHEMICALS PRODUCED BY THE VARIOUS ENERGY TECHNOLOGIES, WILL DO TO THEIR HEALTH AND TO THE ENVIRONMENT.

TODAY'S HEARING SHOULD PROVIDE THE SUBCOMMITTEE WITH AN OVERVIEW OF THE DOE'S CANCER RELATED RESEARCH PROGRAM, AND THE IMPACT OF THE ADMINISTRATION'S PROPOSED FY 1985 BUDGET REQUEST.

NOW, I WOULD LIKE TO RECOGNIZE MY DISTINGUISHED COLLEAGUE FROM NEW YORK, THE RANKING MINORITY MEMBER OF THIS SUBCOMMITTEE, MR. MCGRATH, FOR ANY STATEMENT HE MAY WISH TO MAKE..

I WOULD LIKE TO WELCOME OUR WITNESSES TODAY.

WE WILL BEGIN WITH DR. EDWARD ALPEN, OF THE LAWRENCE BERKELEY LABORATORY AND DR. MICHAEL E. PHELPS OF THE UCLA SCHOOL OF MEDICINE.

Mr. SCHEUER. Mrs. Schneider, do you have a statement you wish to make?

Mrs. SCHNEIDER. No, thank you, Mr. Chairman.

Mr. SCHEUER. We are very happy to have with us today my colleague from New York City, Congressman Guy Molinari.

Guy, we are always pleased to have you join with us. Come on up to the witness table.

In this case, as in so many cases in the past, you are one of us and you are preaching to the converted. You are preaching to the choir. There is terrific bipartisan support on this subcommittee for increasing the funding level for several of the Department's energy health projects, including the one at Brookhaven. My distinguished minority colleague, Ray McGrath, our colleague from New York, welcome you. We both welcome your support for our joint conviction that we should provide the additional funding for these important health programs. This subcommittee will report out legislation increasing those programs. So, you are speaking to a very sympathetic audience.

With that word of welcome, let me say that we look forward to hearing your views. Please take as much time as you may need.

STATEMENT OF HON. GUY V. MOLINARI, A U.S. REPRESENTATIVE FROM THE STATE OF NEW YORK

Mr. MOLINARI. Thank you, Mr. Chairman.

I certainly appreciate the kind remarks and the bipartisan spirit that prevails in this subcommittee. There are others at Public Works where we enjoy the same kind of relationship, and I think the Nation benefits from that kind of a bipartisan attitude.

Mr. SCHEUER. I totally agree.

Mr. MOLINARI. I have a number of concerns, Mr. Chairman, about the funding levels and programs proposed for the biological and environmental research programs that I believe warrant close scrutiny by your committee.

As you know, the total fiscal year 1985 OMB budget authority request for the base biological and environmental research program is on the order of $179.3 million. An additional $5 million was added for initiating certain acid rain research, and another $2 million for the Pacific Northwest Laboratory.

My concern is focused on the base BER program request, which represents a decrease of $2.65 million below fiscal year 1984 and a decrease of $15.4 million below the fiscal year 1984 level of effort when inflation is considered. In my opinion and in the opinion of others much much more schooled in the scientific aspects of these problems, reductions along the magnitude I have described will seriously impair the Department's ability to effectively maintain the Federal Government's only long-term research effort that addresses energy related health and environmental issues.

Let me just say that if you look at some of the things I have pointed out in my prepared statement, I think we have a picture of some of the items of great concern. I will just touch on one, the medical hospital at Brookhaven which is one that I have personally observed. I have been there; I have been all through the facility. That is one that has had tremendous achievement for the country. L-Dopa was discovered there. That is the drug used for arthritis and it has been considered a wonder drug. Also the relationship of salt to high blood pressure.

The one that concerns me, I guess the most, because of my own area that I represent is pulmonary toxicology. We only have to look to the Administrator of EPA and the statements that he has made recently concerning his emphasis on particulate matter. They are talking about developing new standards, and he expressed the view that he is not overly concerned with the large particulate matter, but that which is microscopic or respirable, as they term it.

That is the one that I am most concerned about because the body defenses do not permit filtration of these microscopic particles. Mr. Ruckelshaus has recognized that as a serious problem. It is one that has been a matter of great priority at Brookhaven. It is one that I think we all have to look to in the country. It is our hope—I think this is one of the only long-range programs that exist in the country, and that is why I am here today, Mr. Chairman.

The rest of my statement I will be glad to submit for the record. If you have any questions, I would be glad to try to respond.

[The prepared statement of Mr. Molinari follows:]

TESTIMONY OF CONGRESSMAN GUY V. MOLINARI

BEFORE THE

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH

AND THE ENVIRONMENT

OF THE

COMMITTEE ON SCIENCE AND TECHNOLOGY

MARCH 13, 1984

1

MR. CHAIRMAN, I APPRECIATE THE OPPORTUNITY TO ADDRESS YOUR SUBCOMMITTEE TODAY ON THE SUBJECT OF THE DEPARTMENT OF ENERGY'S BUDGET REQUEST FOR FISCAL YEAR 1985. I HAVE A NUMBER OF CONCERNS ABOUT THE FUNDING LEVELS AND PROGRAMS PROPOSED FOR THE BIOLOGICAL AND ENVIRONMENTAL RESEARCH PROGRAM (BER) THAT I BELIEVE WARRANT CLOSE SCRUTINY BY YOUR COMMITTEE.

AS YOU KNOW, THE TOTAL FY 85 OMB BUDGET AUTHORITY REQUEST FOR THE BASE BIOLOGICAL AND ENVIRONMENTAL RESEARCH PROGRAM WAS ON THE ORDER OF $179.3 MILLION. AN ADDITIONAL $5 MILLION WAS ADDED FOR INITIATING CERTAIN ACID RAIN RESEARCH, AND ANOTHER $2 MILLION FOR THE PACIFIC NORTHWEST LABORATORY. MY CONCERN IS FOCUSED ON THE BASE BER PROGRAM REQUEST, WHICH REPRESENTS A DECREASE OF $2,650,000 BELOW THE FY 1984 APPROPRIATION BY CONGRESS AND A DECREASE OF $15.4 MILLION BELOW THE FY 1984 LEVEL OF EFFORT WHEN INFLATION IS CONSIDERED. IN MY OPINION, AND IN THE OPINION OF OTHERS MUCH MORE SHOOLED IN THE SCIENTIFIC ASPECTS OF THESE PROBLEMS, REDUCTIONS ALONG THE MAGNITUDE I HAVE DESCRIBED WILL SERIOUSLY IMPAIR THE DEPARTMENT'S ABILITY TO EFFECTIVELY MAINTAIN THE FEDERAL GOVERNMENT'S ONLY LONG-TERM RESEARCH EFFORT THAT ADDRESSES ENERGY-RELATED HEALTH AND ENVIRONMENTAL ISSUES.

PLEASE ALLOW ME TO GIVE YOU JUST A COUPLE OF EXAMPLES OF HOW THE PROPOSED FUNDING LEVELS STRIKE AT THE HEART OF SOME OF THE MOST VALUABLE BIOLOGICAL, MEDICAL AND ENVIRONMENTAL RESEARCH EVER UNDERTAKEN IN THIS COUNTRY. IN ORDER TO ACCOMODATE THE OMB BUDGET

LEVELS, A NUMBER OF CRITICAL EFFORTS WILL HAVE TO BE ELIMINATED. FOR ILLUSTRATIVE PURPOSES, HOWEVER, I WILL CONCENTRATE ON THE REPERCUSSIONS OF THE FOLLOWING ACTIONS THAT ARE PROPOSED IN THE BUDGET:

-- FIRST, THE TERMINATION OF CONTRACTS FOR DOE-SUPPORTED LABORATORIES AT THE UNIVERSITY OF ROCHESTER, THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES, AND THE UNIVERSITY OF CALIFORNIA AT DAVIS.

-- SECOND, A SIGNIFICANT REDUCTION IN THE BASIC, APPLIED AND CLINICAL RESEARCH IN PULMONARY BIOLOGY AT BROOKHAVEN NATIONAL LABORATORY, AND THE ACTUAL CLOSING OF THE BROOKHAVEN HOSPITAL AND MEDICAL RESEARCH FACILITY AND CONVERTING IT TO AN OUT-PATIENT FACILITY.

IT MIGHT BE EASY, MR. CHAIRMAN, TO THINK ABOUT CUTS FOR PROGRAMS AND INSTITUTIONS THAT MIGHT NOT HAVE PERFORMED UP TO EXPECTATIONS. YET, FOR THESE FOUR INSTITUTIONS I CAN ONLY SAY THAT THEIR CONTRIBUTION TO OUR SOCIETY AND TO INDIVIDUAL AMERICANS, THROUGH THE APPLICATION OF SCIENCE, HAS BEEN NOTHING SHORT OF REMARKABLE. I THINK IT IS EXTREMELY IMPORTANT THAT WE REALIZE THE CONTRIBUTIONS THAT HAVE BEEN MADE. I AM SURE THAT WE WILL LOOK AT THE BUDGET CUTS DIFFERENTLY IF WE DO SO.

JUST LOOK FOR A MOMENT AT THE ACCOMPLISHMENTS OF THE DOE LAB AT THE UNIVERSITY OF ROCHESTER:

-- IT HAS BEEN A PIONEERING INSTITUTION IN THE FIELD OF LUNG INHALATION TOXICOLOGY;

-- IT DID EARLY STUDIES ON THE METABOLISM AND DISTRIBUTION OF PLUTONIUM AND RADIOACTIVITY IN GENERAL;

-- IT HAS PIONEERED THE CONCEPT OF REPAIR AND PARTIAL REPAIR OF RADIATION INJURY;

THE LAB AT UCLA HAS MADE CONTRIBUTIONS OF EQUAL IMPORTANCE:

-- BY CONTRIBUTING TO THE KNOWLEDGE OF CELL PROLIFERATION AND DIFFERENTIATION AS AFFECTED BY ENERGY-RELATED POLLUTANTS;

-- THROUGH CONDUCTING ECOLOGICAL PROCESS STUDIES AS TO WHETHER CERTAIN ENERGY TECHNOLOGIES ARE FEASIBLE IN CERTAIN AREAS; AND

-- BY EXAMINING THE FUNCTION OF THE BRAIN AND HEART AS MEASURED BY POSITRON-EMITTING RADIOACTIVE MATERIALS (IN OTHER WORDS, ALLOWING CLOSE EXAMINATION OF THESE WONDEROUS ORGANS THROUGH NON-INVASIVE, NON-SURGICAL MEANS);

THE DOE LAB AT THE UNIVERSITY OF CALIFORNIA AT DAVIS HAS ALSO BESTOWED NUMEROUS BENEFITS ON SOCIETY. SOME OF ITS CONTRIBUTIONS HAVE BEEN:

-- LONG-TERM STUDIES OF THE EFFECTS OF THE RADIOACTIVE MATERIALS STRONTIUM AND PLUTONIUM ON BONE. (THESE STUDIES ARE ESSENTIAL TO STUDYING THE RISK OF CANCER FROM EXPOSURE TO RADIOACTIVE SUBSTANCES);

-- EXTENSIVE STUDIES IN THE METABOLISM OF RADIOIODINE, WHICH IS A SUBSTANCE THAT WOULD LIKELY BE EMITTED IN A NUCLEAR ACCIDENT;

-- STUDIES INTO THE MECHANISM OF THE BEGINNINGS OF THE PROCESS THAT LEADS TO LEUKEMIA.

FINALLY, THE ELIMINATION OF THE BROOKHAVEN MEDICAL RESEARCH HOSPITAL AND ITS CONVERSION TO AN OUT-PATIENT FACILITY WOULD BE A TREMENDOUS LOSS TO BIOLOGICAL SCIENCE. I VISITED THIS FACILITY LAST YEAR AND CAME AWAY DEEPLY IMPRESSED WITH THE IMPORTANCE AND VALUE OF THE WORK BEING DONE, AND THE SERIOUS DEDICATION OF THE HIGHLY QUALIFIED STAFF. JUST LOOK AT THE TREMENDOUS CONTRIBUTION OF THIS INSTITUTION:

-- THE MAGNIFICENT DISCOVERY OF THE TREATMENT OF PARKINSON'S DISEASE WITH THE SUBSTANCE L-DOPA, WHICH HELPS ELDERLY

PEOPLE WITH THIS DEGENERATIVE DISEASE TO LIVE USEFUL LIVES. AND THE DISCOVERY WASN'T LIMITED TO THIS ONE TREATMENT; THIS APPLICATION OF L-DOPA POINTED TO THE POSSIBILITY THAT OTHER CHEMICALS COULD BE FOUND WITH WHICH OTHER NEUROLOGICAL DISEASES, PREVIOUSLY THOUGHT IRREVERSIBLE, COULD BE TREATED;

-- BROOKHAVEN WAS A PIONEER IN THE RELATIONSHIP OF SALT TO HYPERTENSION IN MAN. THEIR STUDIES BEGAN IN THE EARLY 1960'S AND CONTINUED UNTIL THE EARLY 70'S. ONLY IN RECENT YEARS WAS THE SIGNIFICANCE OF THIS WORK APPRECIATED;

-- THE FACILITY ALSO PIONEERED STUDIES ON CELL PROLIFERATION IN HUMAN DISEASES, AND THE REGULATION OF RED BLOOD CELL PRODUCTION IN DISORDERS OF THE LUNG;

-- THERE WAS ALSO A BREAKTHROUGH IN THE DETERMINATION OF TOTAL MINERAL CONTENT IN THE BODY BY NON-INVASIVE TECHNIQUES. THIS PROCESS CAN HELP US, FOR EXAMPLE, TO DETERMINE WHAT FACTORS INFLUENCE THE WEAKENING OF BONES IN OLDER PEOPLE BY ANALYZING CALCIUM CONTENT. WE CAN ALSO MEASURE AMOUNTS OF EXCESS RED BLOOD CELL DESTRUCTION THROUGH ACCUMULATIONS OF IRON IN THE BLOOD.

ANOTHER PROGRAM THAT WILL BE TERMINATED UNDER THE PROPOSED BUDGET IS THE HEALTH AND ENVIRONMENTAL RISK ANALYSIS PROGRAM. BY PROVIDING DECISION MAKERS LIKE OURSELVES WITH THE INTERPRETATIONS OF

IMPORTANT SCIENTIFIC DATA, THIS PROGRAM HAS ENABLED US TO MAKE INFORMED DECISIONS ON THE ENVIRONMENTAL AND HEALTH IMPLICATIONS OF ENERGY-RELATED PROPOSALS. IN MY OWN DISTRICT, I HAVE EXPERIENCED THE VALUE OF THIS WORK IN TWO AREAS THAT AFFECT THE HEALTH OF MANY AMERICANS: POWER PLANT SITING AND COAL CONVERSION.

THE COROLLARY, MR. CHAIRMAN, TO THE MANY ACCOMPLISHMENTS I HAVE JUST DESCRIBED IS THAT WE CAN EXPECT MORE OF THIS EXCELLENCE IN THE FUTURE IF THE PROGRAMS ARE PERMITTED TO REMAIN VITAL. LET ME GIVE JUST ONE EXAMPLE: BY ADHERING TO THE BER FUNDING LEVELS SUGGESTED BY OMB WE COULD BE FOREGOING THE ENORMOUS POTENTIAL OF STUDIES IN INHALATION TOXICOLOGY. THESE STUDIES CAN HELP US UNDERSTAND THE IMPACT AND RELATIONSHIP OF INHALED PARTICLES ON CONDITIONS SUCH AS EMPHYSEMA, CHRONIC BRONCHITIS, PULMONARY FIBROSIS, AND CANCER OF THE LUNG. THESE EFFORTS ARE NOT DISSERTATION TOPICS TO BE FILED AWAY IN A UNIVERSITY PROFESSOR'S LIBRARY. THEY PRODUCE RESULTS THAT ALLOW MANY OF US TO LIVE HEALTHIER AND SAFER LIVES.

FOR THE REASONS I HAVE DESCRIBED, I BELIEVE IT WOULD BE A SERIOUS MISTAKE TO FUND THE BER PROGRAM BELOW FY 1984 LEVELS. MOREOVER, RELATIVE TO THE BENEFITS OF THESE PROGRAMS I CAN'T SEE HOW THE COSTS ARE OVERLY BURDENSOME. IF WE RECOGNIZE THAT THE EFFORTS I HAVE DESCRIBED ARE VALUABLE, AND I BELIEVE WE DO, THEN WE MUST SHOW THIS APPRECIATION AND FORESIGHT BY CONTINUING TO APPROPRIATELY FUND THE BER PROGRAM.

Mr. SCHEUER. We are delighted that you did appear here today and give us your views. Anything that we can do to fortify a spirit of bipartisanship in this House as it affects not only our science and technology policy, but as it affects the budget and questions of expenditures on the military and so forth. I think that is what the people want. I think that is what the country is ready for. I think the country is fed up with bipartisan bickering, and they want answers to our problems. I think you have taken a very statesmanlike posture here and you have expressed yourself articulately and with great conviction. I very much appreciate it.

My colleague from Rhode Island.

Mrs. SCHNEIDER. I just wanted to ask if you happen to have any concern about the fact that the budget for risk analysis is essentially zeroed out in this budget. Given your interest and participation in such concerns as risk analysis and also epidemiological studies, do you have any comments to share with us on that?

Mr. MOLINARI. I know the gentlewoman's feelings on that subject, and I think I share them. I am very, very much concerned. I think that is an area where we should be paying more attention. We have even conducted some studies of our own in a very rudimentary fashion, but we were able to come up with some results that indicated to us that there was a problem where governmental agencies told us there was none. So, I have very serious concerns in that area.

Mrs. SCHNEIDER. When you say that we conducted a study ourselves, who are you referring to?

Mr. MOLINARI. I have some environmentalists on staff. We used to work with the city department of environmental protection. We had some problems in my congressional district. We had to do epidemiological studies ourselves, in consultation with others. We even hired some professional consultants to help us in that effort, and we came up with some rather startling results. So, I do know from first-hand observation that this is an area that has to be looked at, and for very little dollars it can produce tremendous results.

Mrs. SCHNEIDER. Thank you very much.

That is all, Mr. Chairman.

Mr. SCHEUER. Mr. MacKay.

Mr. MACKAY. I have no questions, Mr. Chairman.

Mr. SCHEUER. Congressman, I would invite you, very happily, to come up here and sit with us and hear the testimony of Dr. Trivelpiece and perhaps ask him some questions.

Mr. MOLINARI. I welcome that opportunity. I might stay for a bit. Thank you.

Mr. SCHEUER. Excellent. Come right up here. Thank you very much for your testimony.

Dr. Trivelpiece, Director of the Office of Energy Research of the Department of Energy. As I related to the witness who preceded you, your testimony will be printed in full in the record, so if you could sum it up in about 8 or 10 minutes, we would be very grateful, and I am sure we will have some questions for you.

STATEMENT OF DR. ALVIN W. TRIVELPIECE, DIRECTOR, OFFICE OF ENERGY RESEARCH, DEPARTMENT OF ENERGY; ACCOMPANIED BY DR. CHARLES EDINGTON, ASSOCIATE DIRECTOR, OFFICE OF HEALTH AND ENVIRONMENTAL RESEARCH

Dr. TRIVELPIECE. Thank you, Mr. Chairman. I have asked Dr. Edington who is the Associate Director of the Office of Health and Environmental Research to accompany me here today.

Last week, you heard from outside witnesses on this subject area. I have read their testimony. I believe they did a fine job. I don't necessarily agree 100 percent with all the parochial interest they may have expressed, but they did a thorough job in covering the technical material.

Last year, at this hearing, I mentioned the fact that I had commissioned a study of activities that have taken place in the biology environmental research area, and this included what kind of accomplishments have occurred as a result of this program's activities. With your permission, Mr. Chairman, we do have that document complete. I believe members of your staff have it. I would be happy to supply it for the record if you would like. It lists the accomplishments of the Health Environmental Research Program over quite a span of years and goes back into some of the history of the activities related to nuclear medicine.

[The material referred to follows:]

BIOLOGICAL AND ENVIRONMENTAL RESEARCH ACCOMPLISHMENTS

The booklet "Health and Environmental Research: Summary of Accomplishments" provides perspective on the role and contributions of the Department's, and its predecessors' research program. In addition, we have included a compilation of selected accomplishments reflecting more recent research efforts supported by the Office of Health and Environmental Research.

OFFICE OF ENERGY RESEARCH

SELECTED ACCOMPLISHMENTS FOR THE
HEALTH AND ENVIRONMENTAL
RESEARCH PROGRAM

A. Source and Dose Determination

New Measurement Techniques with Lasers

o Organic Constituents in Stack Effluents

During this past year, major advances have been made in the application of lasers in environmental and health research. Scientists at the Ames Laboratory, in collaboration with the Morgantown Energy Technology Center, have been able for the first time to measure complex organic compounds directly in the effluents from a fluidized bed combustor. In this technique, a portion of the stack emission gases are expanded through a supersonic nozzle. The cooled gas is excited with an appropriate laser and emits light which can be analyzed to determine the constituents of the gas steam. Development of an on-line analytical instrument to monitor hazardous compounds in the off-gases and to control such emissions may now be possible.

o Surface Chemistry Reactions

A highly sensitive technique for probing the optical and thermal properties of solids, surfaces and thin films has been developed by scientists at the Lawrence Berkeley Laboratory. The technique, called photothermal displacement spectroscopy, involves focusing a laser beam onto the surface of a sample. The heated sample then expands resulting in a displacement of the surface which can be measured by the reflection of a second laser beam probe. One of the advantages of this technique is its ability to distinguish between surface effects and effects contributed by the bulk material. Although the technique was developed to study chemical transformations on the surface of environmental particulates it can also be applied to characterization of thin films and coatings during the deposition process. Industry has shown interest in the latter application.

o Analysis of Biological Fluids

A straightforward method for the detection of extremely small quantities of many biologically active substances in liquids has been developed at the Los Alamos National Laboratory. The method is based on the measurement of laser-induced fluorescence with an instrument designed for flow cytometry. A laser probe has been developed which can excite picoliter volumes of a slowly flowing liquid sample stream. The induced fluorescence is detected with microscope optics and filtered to reduce scattered laser light. As few as 35,000 molecules flowing through the probe volume can be detected, nearly two orders of magnitude better sensitivity than previous flow cell measurements. It is anticipated that this new technology will become increasingly important in biological research where detection of small numbers of receptors or binding sites is required.

o Uranium Monitoring in the Workplace

Scientists at the Pacific Northwest Laboratory have developed a method for measuring uranium concentrations in bioassays more quickly,

easily and accurately than conventional chemical methods. The new technique, called kinetic phosphorimetry involves illuminating the sample with a high intensity laser pulse. Uranium, in the form of a phosphate complex, absorbs the light and re-emits it at a different specific wavelength. This phosphorescent emission is measured after a 50 microsecond delay. Both positive and negative interferences can be corrected for. Uranium can be measured at the parts per billion level with accuracy greater than three percent. Potential applications of the method include routine monitoring of workers in the uranium mining, milling and processing industries, monitoring of reactor cooling water at nuclear power plants and environmental monitoring.

Characterizing Toxic Components in Synthetic Fuels

The Office of Health and Environmental Research, during the course of its research on synthetic fuels, has developed a unique cost-effective approach for assessing the potential health impacts of these complex chemical mixtures. This approach, called bio-directed analytical characterization, uses a combination of sophisticated chemical separation techniques and short-term biological assays to identify these components of complex chemical mixtures which exhibit biological activity and are, therefore, of potential concern to human health. Using this approach, OHER has been able to show that of the several thousand chemicals present in complex synthetic fuels only two classes of compounds are of biological concern from a carcinogenic point of view, namely polynuclear aromatic hydrocarbons, and nitrogen containing polynuclear aromatic hydrocarbons. Technology developers are currently using this cost-effective bioanalytical characterization technique to investigate process variations designed to eliminate biologically active components of synthetic fuels.

It is anticipated that the technique will receive wide application in all industries concerned with biological activity of complex chemical mixtures.

B. Environmental Fate and Behavior

Atmospheric Modeling Studies Serve Multiple Uses

The transport and dispersion models that were developed as part of the Atmospheric Studies in Complex Terrain (ASCOT) studies in The Geysers area of California are being used by the California Air Resources Board in evaluating the siting and extent of future geothermal development in The Geysers. ASCOT is an ongoing research program with theoretical, laboratory and field components that is developing a better understanding of atmospheric dispersion in complex terrain. Currently the field research is focused on the oil shale area of western Colorado. The ASCOT model developments have also been incorporated into the Atmospheric Release Advisory Capability (ARAC) system of Livermore and similarly by the Savannah River Laboratory for their site emergency response system.

Both of these systems are designed primarily to simulate the fate of atmospheric releases resulting from nuclear accidents, but are equally applicable to non-nuclear accidents.

Cross-Appalachian Tracer Experiment (CAPTEX)

For the first time, scientists have been able to chart the air motions over the Northeast United States and Southeastern Canada in sufficient detail to begin to answer some of the questions posed by large scale atmospheric pollution issues such as "acid rain." The Department of Energy's "Cross-Appalachian Tracer Experiment," called CAPTEX for short, made use of a newly developed, chemically inert tracer gas. This tracer material was injected into the atmosphere in Ohio and Sudbury, Ontario, in seven individual tests during September and October of 1983. After its injection, the tracer gas was spread by the prevailing winds and was sampled by seven aircraft and over 80 additional samplers on the ground as it traveled eastward and passed off the east coast. The 3000 or more samples collected during seven releases of the tracer gas will be analyzed for tracer gas concentration at two Department of Energy laboratories. These analyses, along with the simultaneously-collected meterological data, will be made available to atmospheric scientists by mid-1984. The details of that movement, as determined from the gas concentrations measured at the sampling sites, will furnish information which atmospheric scientists can use in testing and developing mathematical models of the regional scale transport and dispersion. These models are used to determine which sources of atmospheric pollutants affect which sensitive regions downward.

The Department of Energy began the tracer development program eight years ago. The 1983 CAPTEX experiment was conducted in coordination with the National Oceanic and Atmospheric Administration, the Environmental Protection Agency, the Electric Power Research Institute, the Atmospheric Environment Service of Canada, and the Ontario (Canada) Ministry of the Environment.

Understanding the Formation of Acid Precipitation

Previously, it was believed that hydrogen peroxide (H_2O_2) and possibly other organic peroxides were the principal chemicals involved in the conversion of sulfur dioxide (SO_2) to sulfuric acid in cloud and fog droplets. It was assumed by the atmospheric chemistry community that these compounds originated solely from photochemical reactions in the atmosphere. However, investigators at Lawrence Berkeley Laboratory have recently demonstrated in laboratory experiments that incomplete combustion of fuels is a significant source of H_2O_2 and organic peroxides. Complete combustion of the same fuels does not produce these compounds. This finding, although new, is important in understanding the context of atmospheric chemistry, because it links the chemistry involved in transformation of energy-related pollution to the type and/or quality of combustion. This research also points out the need for studying the emissions and properties of nonregulated chemically reactive pollutants, such as peroxides, because droplet acidification may depend more critically on them than on the concentration of sulfur dioxide in the atmosphere. Because peroxides are

emitted from incomplete combustion, mobile sources as well as other local sources (home heating, wood burning) may play a significant part in providing acid precipitation. The results of this research have important implications with regard to health effects, emissions regulations, and environmental controls.

Advances in How Ecosystems Function Clarifies Effects of Acid Rain

Fundamental research on the functioning of ecological systems is providing answers to many of the questions underlying current environmental issues. The several research projects discussed below were designed to provide fundamental knowledge of how and why natural processes operate as they do. However, they also provide insight for understanding and interpreting current environmental issues, such as acid rain and trace metal contamination of soils.

Research supported at Dartmouth and the University of Maine has made a major contribution to understanding the effects of acid rain on lakes. The work revealed that acid rain mobilizes aluminum, a common constituent of soils and sediments. Studies were initiated in 1977 because DOE staff projected that possible long term effects of acid precipitation would stem from acceleration of the breakdown of soil minerals, a process which occurs naturally but at a slow rate over a long period of time. The work has revealed that increases of soluble aluminum in lakes to toxic levels account for the decline in fish populations in some lakes. The increase in aluminum is believed to be due to an increased rate of release of aluminum from soils and sediments caused by acid precipitation. This finding has caused others to examine the chemical processes which take place in landscapes surrounding sensitive lakes, and should lead to a sounder basis for prescribing remedial actions which are more cost-effective.

ORNL scientists and a collaborator from Dartmouth College have described the processes by which fog reacts with plant leaves to accelerate deposition of atmospheric pollutants. The conifer needles and surrounding water droplets contained in fog interact at high altitudes so that deposition of atmospheric acids is considerably higher than previously thought. They believe that this phenomenon accounts for damage to conifers at higher elevations which is greater than would be expected for the existing levels of air pollution.

In soils, this research team has shown also that the extensive surfaces provided by soil particles in clay can be a key factor in the retention of acid sulfates in the soil itself. By absorbing sulfate, these soil particles immobilize the sulfur compounds and prevent the loss of valuable nutrients from the soil as well as potentially toxic materials, such as aluminum, which was mentioned above.

Radionuclide Uptake From Pasture to Milk

Scientists in the Environmental Sciences Division, at the Oak Ridge National Laboratory have tested the validity of a mathematical model that is used to calculate the estimated internal radiation dose to humans who have

ingested milk from cows or goats grazing on pasture contaminated by radioactive isotopes. The model is documented in Nuclear Regulatory Commission Regulation Guide 1.109 and is representative of models now employed by radiological health organizations. The model consists of equations which estimate the amount of radioactivity that is transferred from soil to plant to cow or goat to milk.

The field experiments with grazing goats gave results for three important radioisotopes. Iodine-131 that was deposited on pasture grass was transferred to milk in reasonable agreement with model predictions. In another pasture, where the soil was contaminated with cesium-137, the transfer through the soil-pasture-goat-milk pathway also validated model predictions. However, experiments with technetium-95 indicated that the predicted milk concentrations are high by about 1000 fold. This discrepancy is due to a chemical change in the technetium after deposition on vegetation which makes it less soluble than in its aerosol form.

Oceanographic Model Predicts Space Shuttle Debris

Future space shuttles from Cape Canaveral will be launched with large reservoirs of oxygen and hydrogen. When the shuttle is in orbit, it will be powered by Pu^{238} fueled radioisotope thermoelectric generators (RTG). There is a remote possibility that an accident during launching could result in RTG fuel being dispersed into the atmosphere and oceans adjacent to the Cape. Key questions concerning the dispersion of Pu^{238} fuel includes where does this radioactivity go in this environment and what is the dose to people living in this area from exposure due to a launch accident? Models to provide answers to these questions were recently used in Environmental Impact Statements by both DOE/Space Nuclear Systems and Environmental Assessments by DOE/Savannah River Plant for the startup of "L" reactor.

The oceanographic information developed by DOE/OHER/ERD's regional marine research program in the Southeast Atlantic Ocean was key in developing the transport and dispersion model of Pu^{238} for these assessments. The regional marine programs have broadly focused on an improved understanding of the structure and functions of the natural marine system into which a variety of impacts from energy-related activities must be determined.

Arctic Research Also Serves Grasslands Region

As a part of a research program on potential responses of Arctic tundra to changes from energy development, a research group at San Diego State University has developed a computer-based model, the Arctic Tundra Simulator (ARTUS). This is an ecosystem model which simulates basic plant and soil processes in tussock tundra of Northern Alaska that could be altered by energy development.

Although the model was developed from Arctic research, it is being used as a basis for an agricultural model to simulate the behavior of single grass species to any of the many models developed from work within the grasslands region.

Although the Arctic environment seems far removed from the environment of short grass prairies, this study demonstrates that some basic ecological processes are more readily revealed in the less complex Arctic, and when these processes are understood they can be successfully transferred to other more complex areas such as the grasslands.

Detoxification Mechanisms by Marine Shellfish

Whether or not accumulated pollutants are harmful to the animal is largely determined by the organism's ability to metabolically transform them into more water-soluble (detoxified) forms. Conversely, some metabolic transformations result in the production of activated compounds that are more toxic than the original pollutants. A model aromatic amine (o-toluidine) was used in the experiment because its structure is representative of a broad class of potentially mutagenic compounds.

Live shellfish were found to rapidly accumulate o-toluidine and eliminate metabolites that were significantly different from those produced by vertebrate organisms. In addition to the production of activated (N-oxidized) metabolites, these organisms were able to add a single carbon atom to the nitrogen and form a novel detoxification product, N-formyl-o-toluidine. This nitrogen metabolizing pathway represents a significant departure from the two-carbon addition (acetylation) that is usually observed in vertebrate species. The common carbon-oxidizing metabolic pathways expected to occur in mammals were verified in a rat but never occurred in the molluscs studied. The metabolic pathways utilized by these shellfish serve to point out the distinct differences in their detoxification capabilities.

The experimental protocols developed by Lawrence Livermore National Laboratory in this study will be used to directly assess the metabolic processing of a variety of pollutants by marine invertebrates. This basic information on processes is necessary because our knowledge of chemical metabolism is largely based on studies of vertebrate organisms and may not directly apply to food species.

C. Health Effects Studies

New Findings from Studies of Atomic Bomb Survivors

Recently published reports from the Radiation Effects Research Foundation (RERF) present important findings on the relationships between cigarette smoking and radiation exposure associated with cancer mortality, and between radiation exposure and age associated with ophthalmologic changes.

Cancer mortality among 40,498 Hiroshima and Nagasaki residents was examined in relation to cigarette smoking habits and estimated exposure to atomic bomb radiation. Persons heavily exposed to both cigarette smoke and radiation were found to have significantly lower cancer mortality than synergistic models would suggest for all nonhematologic cancer as a group, for stomach cancer, and for digestive cancer other than stomach cancer.

Surprisingly, the joint risk for smoking and radiation exposure for these cancers appeared to be less than the individual risks added together. Even the risk of lung cancer could not be distinguished from either a synergistic (multiplicative) or an additive form.

Radiation damage to the human lens usually appears after a latent period of several months to several years, sometimes first appearing only later in life. One of the earliest radiation effects observed in the A-bomb survivor population was the occurrence of lenticular changes, but it was unclear whether the lenses of young persons are particularly susceptible to radiation-induced lenticular opacities, particularly at doses less than 200 rad. A recently completed two-year study indicates that increased abnormal lens findings are associated with increasing age (as part of the normal aging process), and that this association appears to be stronger for persons exposed early rather than late in life in Hiroshima but not in Nagasaki. This discrepancy may be due to observer bias or differences in radiation exposure in the two cities. There did not appear to be a statistically significant risk of opacities at doses less than 200 rad.

Reassessment of Survivor Radiation Exposures at Hiroshima and Nagasaki

The reassessment of the radiation exposures of survivors of the A-bomb at Hiroshima and Nagasaki now in progress, is expected to lead to the assignment of definitive radiation doses to individual survivors and survivor groups. These results, when coupled with the health effects data base developed during the past three decades, will yield the most reliable estimates of human health risks from acute radiation exposure. During the past year, the uncertainty in the explosive yield of the Hiroshima weapon has been reduced, the nature of the fission products, neutron and gamma radiation released by that weapon more accurately determined, and their dispersal patterns in air calculated. In addition, considerable progress was made in both designing a model to calculate shielding characteristics of the housing clusters present in Hiroshima at the time, along with some other relevant parameters needed to ascertain the dose estimates for exposed individuals. By late 1984, all this information will be used by the Radiation Effects Research Foundation in Hiroshima to establish the actual dose determinations.

Non-Confirmation of Reported Carcinogenic Effects of Internal Radium

Reports explicitly linking radium in the human body with breast cancer and multiple myeloma have recently appeared in the literature and the assumption of an association with leukemia has been present in the literature for some time. Recently published results from the study of the U. S. radium dial painters cast doubt on these assumed relationships. The Center for Human Radiobiology at Argonne National Laboratory compared rates of multiple myeloma and leukemia among female radium dial workers with those expected from U. S. white female rates. Dose-response relationships of the rates of these cancers to the amount of radium that got into the body were determined in those workers whose body contents of radium had been measured after 1955. A three-fold excess risk of multiple myeloma occurred in the pre-1930 group, however, analyses of radium contents and durations of

employment suggest that radiation from sources outside the body was more likely to have been responsible than was radium inside the body in the occupational environment. Extensive analyses of information on breast cancer uncovered several observations strongly weighing against a causal interpretation of the association between body contents of radium and breast cancer. Leukemia incidence and mortality have not been elevated overall among the female dial workers, either in the pre-1930 or the post-1930 groups.

Biological Effects of Low Level Exposure to Neutrons

There has been some recent controversy about proposed changes in the maximum allowable human exposures to neutron radiation. First, reanalysis of the doses received by the Japanese A-bomb survivors suggests that the neutron component of the exposure was less than originally thought. Thus, no human data are available to evaluate the relative effectiveness of neutrons and gamma rays for life-span reduction or tumor production. The value for the relative biological effectiveness (RBE) of neutrons compared to gamma radiation is presently considered to be about 10, and exposure standards are based on that number. Early experimental data suggested that the relative biological effectiveness of neutrons increases at low levels of exposure. More recent data suggested that the relative effectiveness in the low-dose range increases to even higher values when the exposures were protracted in time.

New data have been obtained from a large experiment at Argonne National Laboratories, which compared the relative effectiveness of neutrons and gamma rays for life-span reduction and tumor production. These data indicate that at low level exposure, approaching those that might be encountered by human beings, there is no increased effect when neutron exposures are protracted over long periods of time. This finding suggests that if any modification in the maximum allowable dose is warranted, it would be a small one.

Mechanism of Radiation Induction of Leukemia

Aplastic anemia and myelogenous leukemia can be consequences of human exposure to ionizing radiation, certain medicinal drugs, and industrial chemicals. Both are life-threatening diseases that result from damage to cells of the hematopoietic (blood-forming) system in bone marrow.

Research at the Argonne National Laboratory has utilized the dog as an experimental model to probe mechanisms underlying these diseases, particularly leukemia. In animals chronically exposed to gamma radiation, radiation dose-rate has been shown to be a critical factor relative to disease induction. Thus, aplastic anemia is the predominant disease at certain dose rates whereas leukemia becomes dominant when the dose rate is lowered. In both cases, there occurs an initial decrease in blood levels of circulating red cells, white cells, and platelets. In aplastic anemia this trend continues and completely destroys the marrow compartment, resulting in early death. If reparative processes restore marrow function, life span is significantly extended, but the risk of leukemia is correspondingly

increased. Observations of a similar nature relative to dose-rate effects have also been reported by contractors at the University of California, Davis.

More recently, the Argonne study has demonstrated that the blood-forming cells in leukemia-prone animals acquire a very efficient, but aberrant (error-prone), repair capacity. In contrast, aplastic anemia-prone animals fail to acquire such an ability. Further analysis of cellular repair in chronically irradiated animals has provided support for the view that acquisition of a modified (aberrant) repair capacity may be a key event in the induction of leukemia by ionizing radiation.

Since canine and human myelogenous leukemia are similar diseases, the ability to monitor the repair capacity of blood-forming cells in bone marrow may permit identification of individuals who are prone to radiation-induced leukemia. Better understanding of mechanisms of hematopoietic cells damage and recovery may lead to better diagnosis, treatment, and, perhaps, prevention of associated life-threatening blood diseases.

Effectiveness of Daily Chelation (Drug) Therapy in Prevention of Plutonium-Induced Skeletal Tumors

On entering the body, plutonium is subject to long-term retention in certain tissues including bone. Prolonged retention results in long-term, localized irradiation of tissue cells and increased risk of tumor induction. Research has demonstrated that certain chelating (metal-binding) agents, particularly DTPA, can effect the removal of plutonium from the body. DTPA acts by chemically binding to plutonium in tissues and facilitating its excretion in the urine. In a limited experiment still in progress, investigators at the University of Utah are evaluating the extent, if any, to which DTPA therapy (intravenous injections) actually reduces the risk of bone tumor induction and prolongs life in plutonium-exposed dogs. In this effort, the internal translocation of plutonium from a large deposit in the liver to bone under the influence of DTPA therapy was studied. No treatment resulted in the accumulation of plutonium on bone surfaces and death from bone cancer (osteosarcoma). Daily treatment with the chelator zinc-DTPA led to a dramatic reduction in both liver and skeletal deposits of plutonium. This treatment has also clearly extended the time of post-exposure survival. Although all animals treated with zinc-DTPA are still living, radiation dose rates to sensitive bone cells have been found to be significantly reduced by chelation therapy. Thus, zinc-DTPA administration may prevent or substantially delay formation of bone sarcomas. This experiment, although it involves only a small number of animals, makes a strong case for continuous chelation therapy and for development of an effective and safe plutonium chelator that can be taken orally every day.

Adaptive Response of Human Lymphocytes to Low Concentrations of Radioactive Thymidine

Whether low doses of radiation affect the response of human cells to subsequent radiation doses has been a matter of controversy. Workers at the Laboratory of Radiobiology and Environmental Health of the University of

California, San Francisco, have recently reported evidence for the adaptive response of human cells to low concentrations of radioactive thymidine (a DNA precursor). When human lymphocytes were cultured in the presence of tritium-labeled thymidine which acts as a source of low-level chronic radiation, and subsequently exposed to 150 rad of x-rays, the yield of damaged chromosomes was less than the sum of the yields of damaged chromosomes induced by the tritium-labeled thymidine and x-rays separately. Often fewer damaged chromosomes were found after exposure to radiation from both sources than were found after exposure to x-rays alone. Nonradioactive thymidine did not affect the yield of x-ray-induced damage. It thus appears that low levels of chronic radiation can trigger or induce increased repair of radiation-induced chromosome breaks. This response is similar to the adaptive response to chemicals which damage DNA that has been reported by others. In those experiments, cells chronically exposed to small doses of a DNA-damaging chemical agent were resistant to subsequent exposures to large acute doses of the same chemical.

Lung Response to Inhaled Diesel Exhaust Emissions

Research in progress at the Lovelace Inhalation Toxicology Research Institute is providing valuable information on responses induced in the pulmonary system by chronic inhalation exposure to the complex, heterogeneous mixture of chemicals present in diesel exhaust emissions. In this study, rats and mice have been exposed over a 24-month period to graded levels of diluted diesel-engine exhaust. Low levels of exposure (ten times expected population exposure levels, corresponding to 0.35 mg/m^3 of diesel exhaust particles) did not result in progressive accumulation of exhaust particles in the lungs and had no detectable deleterious effects on the lungs. At higher levels of exposure (100 times expected population exposure level, 3.5 mg/m^3 of particles), the capacity of the lungs to clear respirable particles was exceeded and a progressive accumulation of particulate material resulted. This effect was accompanied by chronic pulmonary inflammation, patchy pulmonary fibrosis, and pulmonary function changes. No lung cancer has been observed to date. Completion of this study will provide important insights into the toxicity of complex chemical mixtures and valuable information on the need for particulate emission standards for automotive exhaust emissions.

New Finding on Toxicity of Complex Coal Conversion Material

Recent results obtained at Argonne National Laboratory and the Pacific Northwest Laboratory have demonstrated that the cancer-producing activity of certain chemicals in tar by-products of coal conversion processes is reduced by non-toxic components of the same chemical mixture. This finding suggests that predictions of health risk based on consideration of only the most toxic component or even the summation of the toxicity of the individual components is not valid. The finding results from research to discover which components of complex materials are responsible for adverse delayed effects such as cancer production. As part of that work, crude materials are chemically separated into fractions that represent different classes of chemicals. When such fractions were painted on the skin of mice and their activity compared with that of the crude material, the mice exposed to the

crude material developed fewer malignant tumors than did those that were exposed to the separated fractions. In that regard, a recent report prepared by the National Academy of Science Engineering and Public Policy highlighted the national need to evaluate the adverse health effects of complex mixtures as well as those of individual chemical compounds.

D. Basic Biology

The National Synchrotron Light Source Provides New Tools for Basic Biological Research

The National Synchrotron Light Source (NSLS) facility at Brookhaven National Laboratory is a unique source of electromagnetic radiation that allows new approaches to the study of the structure of complex biological materials. Special instrumentation has been created to carry out a wide range of biophysical studies.

Ultraviolet-visible spectroscopy can measure the absorption, fluorescence, or polarization of light from such materials as DNA molecules and the tryptophan residues in proteins. This should significantly improve our determinations of the secondary structure (molecular conformation) of biological macromolecules. Other kinds of spectroscopy can be extended into the vacuum ultraviolet where more conventional sources of radiation have low intensity.

Soft x-ray microscopy of biological samples can become a practical technique as soon as the tunable synchrotron source becomes fully operational. At certain x-ray wavelengths, biological tissues appear relatively opaque while water is transparent. The soft x-ray microscope offers potentially a 100-fold improvement in resolution over the visible light microscope.

Extended x-ray absorption fine structure (EXAFS) is another experimental technique which has developed at the NSLS. An example of its usefulness in biology is that of determining structural and chemical characteristics of the metal-binding sites in metalloproteins such as hemoglobin (an animal protein) and nitrogenase (a plant protein).

Neutron Diffraction and Scattering

The physical structure and chemical activity of proteins depend strongly on their hydrogen atoms, so knowing the precise location of the hydrogen atoms is necessary for understanding both the structural and chemical properties of proteins. The technique of X-ray diffraction has the basic limitation that because of their extremely low scattering of x-rays, hydrogen atom positions are not directly observable and must be inferred from the stereochemistry (spatial location) of the heavier atoms. In contrast, hydrogen atoms are readily located in neutron diffraction studies because of their relatively large neutron scattering potential. The development of two-dimensional position sensitive neutron detector systems has also had an important impact on the field because they allow the simultaneous collection of data from many points.

A neutron analysis of the enzyme trypsin was done at Brookhaven National Laboratory to try to resolve a much debated issue on the mechanism of the serine protease family of enzymes. Specifically, the debate centered about the question as to which of two groups in the protein's active site acts as the catalytic group during the reaction. The neutron study demonstrated conclusively that the catalytic group was the imidazole group of histidine-57 and not the carboxylate group of aspartic acid-102. From this finding, important general conclusions could be drawn about the mechanism of action of this class of enzymes.

The structure of membrane and other macromolecular assemblies that are key functional components of living cells can be determined by low angle neutron scattering. The ribosome, a protein-nucleic acid complex that plays a central role in protein synthesis, has been studied by neutron scattering for several years. Measurements of the three-dimensional structure of ribosomes have progressed to the point where the geography of the distribution of proteins within the ribosome will soon be known, making a major milestone in neutron investigation of macromolecular assemblies.

National Gene Library Project

A joint program has been initiated at the Los Alamos and Lawrence Livermore National Laboratories for the isolation of human chromosomes and preparation of human chromosome-specific DNA inventories or libraries. Human DNA, the chemical in which genetic information is encoded, is organized into 24 chromosome types. For the preparation of chromosomal-specific DNA inventories, DNA from each isolated chromosome will be broken into smaller pieces and these pieces replicated many times. The chromosomal specific libraries will be provided to the scientific community for use in research activities.

The availability of large amounts of chromosome-specific DNA will have a major impact in studies related to human genetics and will provide a foundation for broad and significant advances in both medicine and basic science. In particular, this research will enhance our understanding of chromosome structure, human genetic disease, cancer, gene mapping, actions and strategies for developing new therapeutic agents, the regulation of gene expression during various stages of development and growth, and will provide better approaches to the study of environmental agents which alter human DNA.

Phase I of the project is underway and has as its goal the rapid production and distribution of the inventories for each human chromosome. The first inventories will be available in mid-1984. Phase II collections will contain larger pieces of DNA which will be more useful for certain kinds of investigations.

Chromosome Instability and Carcinogenesis

Tumor cells normally contain abnormalities in their chromosomes. In the case of common solid tumors of mammals, including humans, the specific abnormalities are variable among different tumors of the same type as well

as among the cells of any particular tumor. These facts, known for many years, suggest that chromosomal abnormalities are closely coupled to the neoplastic process. However, two questions concerning chromosome changes in cancer have stubbornly resisted clarification. First, are the chromosome changes a cause of the neoplastic process (which is known to be multistep) or an effect which becomes manifest after the process is well underway? The second question concerns the heterogeneity, cell to cell, often seen in solid tumors derived from a single cell. Are the earliest changes more homogeneous and, if so, are they mechanistically related to the development of chromosome instability seen in cancer cells?

New techniques have been developed at the Los Alamos National Laboratory for studying chromosomes and for analyzing tumor formation in nude (immunologically deficient) mice. These techniques have been applied to study the transformation to a cancerous state of normal Chinese hamster cells which are grown in culture. In particular, this work has shown that chromosomal abnormalities are observable at the earliest stages of the process, a stage that preceeds all conventional indicators of the development of the tumorigenic state. Furthermore, the data support the idea that specific chromosome changes seen at this earliest stage are restricted to a small subset of types that are seen repeatedly in independent cell lines which undergo stepwise neoplastic transformation. The research is currently focused on this early stage of cancer development with the objective of determining whether there is a relationship between the observed early recurring chromosomal changes and the chromosomal location of genes known to be related to the development of cancer (oncogenes).

DNA Repair Capacity and Cancer Susceptibility in Humans

Much experimental evidence supports the view that cancer induction by carcinogenic agents such as ultraviolet (UV) radiation, x-rays (and other forms of ionizing radiation), and certain types of chemicals involves a modification of gene expression. These carcinogenic agents have been shown to cause specific types of damage in DNA molecules, which comprise the genetic material of living cells. Related research has established that cells of many living species contain DNA repair systems that afford protection against such damage. Most of the existing knowledge concerning DNA damage and repair has come from research sponsored by the Office of Health and Environmental Research.

Research performed at the Brookhaven National Laboratory has demonstrated that deficient or defective DNA repair is linked with increased susceptibility to cancer in an experimental animal model (a species of fish). The same type of linkage has also been detected in humans by research conducted at several DOE laboratories (the University of California in San Francisco, Oak Ridge National Laboratory, Brookhaven National Laboratory, and others). This work has established that DNA repair-deficient hereditary diseases in humans are associated with tremendous increases in cancer susceptibility. Most of our knowledge in this area stems from work done on two hereditary diseases, xeroderma pigmentosum (XP) and ataxia telangiectosia (AT). XP individuals are on the

average about 80 percent defective in DNA repair and have a cancer susceptibility about 10,000 times greater than that of the average normal individual. Cancer prevalence is about 100 times greater than normal in AT individuals, but the magnitude of their repair defects is not yet known.

Work recently initiated at Brookhaven will define the variability in DNA repair capacity that exists among individuals in an apparently normal human population. It is also planned to evaluate cancer susceptibility in this population via a long-range follow-up study. Information gained from continuation of this and other human studies should improve capabilities for identifying cancer-susceptible individuals who, for example, should be excluded from work environments that may involve chronic, low-dose exposures to carcinogens. Early diagnosis as well as prevention and/or improved treatment of cancer may also be facilitated.

Differentiation and Gene Expression in Normal and Cancer Cells

The broad question of what factors in the environment of a living cell modulate its gene expression and tissue-specific functions is a central issue of modern cell biology. An important aspect of this research is the analysis of morphogenetic and biochemical changes that accompany the "initiation" and "promotion" steps in two-stage carcinogenesis. Major advances have recently been made at the Lawrence Berkeley Laboratory towards understanding the role of the extracellular matrix in modulating the morphology, biochemical pathways, and functional differentiation in mouse mammary epithelial cells grown in culture. By changing the composition of the extracellular matrix, cells can be made to simulate in culture the metabolic profiles and morphological characteristics of cells from pregnant and lactating mice.

In other studies, the changes in cellular gene expression and protein synthesis that are induced by oncogenic viruses and tumor-promoting agents such as phorbol esters are being revealed through a series of experiments with chick embryo fibroblasts in culture. These investigations have led to the interesting observation that the treatment of fibroblasts with the tumor promotor, TPA, induces changes that are characteristic of cells transformed by Rous sarcoma virus (RSV), a virus which causes tumors in chickens. However, changes in protein phosphorylation in cells treated with TPA are not identical to those observed in RSV-transformed cells. The induction of the transformed state by TPA may therefore proceed by different mechanisms than those which are currently believed to be involved in the action of RSV. An important new finding in this area is that the treatment of fibroblasts with TPA and the transformation of these cells with RSV both lead to increases in the synthesis of the protein subunits of intermediate filaments, the ropelike polymers of fibrous polypeptides that play a structural or tension-bearing role in the cell. Therefore, both TPA and RSV may induce a major reorganization in the network of these intracellular fibers which would be directly related to the acquisition of the transformed or tumorigenic state.

Development of Epithelial Cell Cultures from Human Mammary Gland

The OHER program has emphasized the development and use of human cell and tissue systems in both applied and basic research programs. As part of this effort, a research group at the Lawrence Berkeley Laboratory has recently developed a human epithelial cell culture which can be grown for extended periods of time outside of the body. It has been established that in vitro cultures of these cells show most of the normal functions of the epithelial cells in the functioning gland of human beings. That finding now makes it possible to study, for the first time, the most basic molecular mechanisms of growth and differentiation, as well as regulation by hormones and other factors of enzymes involved in milk production. It is now also possible to study the kinds of cell-cell interactions that regulate or modulate the activity of these cells. In addition, the cell cultures have been shown to respond to chemical carcinogens in a manner similar to that of the epithelial cells in the normal organ, including a greater sensitivity than fibroblast cells derived from the mammary gland. This is a particularly important finding because most human cancer, including over 99 percent of human mammary cancer, is of epithelial origin. For this reason, the human mammary epithelial cell culture is being developed as a model system for the study of mechanisms in the transformation of normal human epithelial cells to the tumorous state, including mechanisms of dedifferentiation processes that typically accompany tumorigenesis.

E. Nuclear Medicine Applications

Heavy Ions in Radiation Therapy

One thousand or so cases of malignant melanoma of the eye are newly diagnosed each year in the U.S. Standard treatment is the removal of the eye immediately upon detection of the tumor. Physicians and scientists at the Lawrence Berkeley Laboratory have been treating this cancer with very precisely localized heavy ion beams. Their success rate is well over 90% for patients with over one year follow-up. They believe that even this can be improved with further research. Furthermore, vision is retained in the affected eye to some degree in all patients with disease control. For the larger fraction of these, visual retention is truly functional and useful. Other therapies, such as the application of radioactive plaques to the outer surface of the eye, are being tested, but are as yet unproven.

Approximately 10,000-20,000 people every year are found to have defects of congenital origin in the circulatory system in the brain, so-called arterio-venous malformations. These defects are life threatening. Many can be treated surgically because their disease is in an accessible location. Many, perhaps as many as 2000-3000 cannot be treated surgically because of inaccessibility of the lesion. At Berkeley and at Harvard these patients are being treated with charged particle beams. In the Berkeley experience well over fifty patients have been treated and none have shown further bleeding. The follow-up must, of course, be much more extended, but the present results are very promising.

Radionuclide Generator Development for Heart Disease

Radionuclide generator systems are used as a convenient source of very short-lived "daughter" radionuclides that are formed by the radioactive decay of a longer-lived "parent." The Oak Ridge National Laboratory has developed a new, improved generator for the radioisotope iridium-191m with a half-life of 5 seconds which has become very important in diagnosing heart abnormalities in both children and adults. Since 1980, the Oak Ridge National Laboratory has supplied the parent osmium-191 radionuclide, with a 15-day half life, to Children's Hospital in Boston where the generators are prepared and the separated iridium-191m is used to evaluate heart disease in children. Advanced gamma-camera imaging systems can take 12 to 15 pictures per second of the radioisotope as it is carried along in the patient's bloodstream. Abnormal passage of blood between the heart chambers can be easily detected and evaluated by this non-invasive technique, and patients identified for surgery. Iridium-191m is particularly well-suited for pediatric use because its ultra-short half-life results in a very low radiation exposure and because its rapid clearance allows repeat studies within a very short time. Some 20,000 children each year in the United States are born with the congenital heart defect that can be diagnosed in this way.

Cardiovascular Disease Detection

Studies with positron emission tomography have been providing a wealth of new information about the metabolic and biochemical basis of human cardiovascular disease, the largest single killer in America. In 50% of people with coronary heart disease, the first symptom is sudden death. Thus, there is an urgent need for a diagnostic technique that is sensitive to the earliest changes that occur in the unsymptomatic stages, and for study of certain risk factors, such as hypertension, smoking, high blood cholesterol and fatty acid levels. Various existing conventional technologies, such as electrocardiography, nuclear medicine studies, angiography, and ultrasound, can diagnose the presence of developed heart disease quite well, although early detection by these techniques is difficult. Detection of mild cardiovascular disease has been demonstrated with positron emission tomography. This technique has also demonstrated its value for the determination of therapy, such as bypass surgery. The important issue is whether tissue is alive and has survived the initial attack. This is a biochemical or metabolic question for which only positron tomography has shown capability to directly make the evaluation. Recently, studies have been carried out in patients before and after bypass surgery. In all cases where it was indicated from positron emission tomography that tissue was not viable, it did not recover. In patients where it was indicated that the tissue remained viable, the patients did recover.

Technique for Screening Antibodies in Living Tissue

Antibodies of interest for diagnosis and therapy are often screened by assessing binding strength in systems substantially different from that which is found in the patient. While studies in animals and humans are the ultimate determinant for success, these are associated with practical obstacles. At the University of California, Davis, they have developed perifusional techniques to provide screening under circumstances closer to that of a patient. When human cancers and normal tissues are placed in a media with cancer-specific radiolabeled monoclonal antibodies, 4-10 times greater specific antibody accumulated in the human tumor. These observations suggest the feasibility of screening antibody against living tissues using this perifusional technique. A potential application of the technique relates to its use for screening cancer removed from patients in order to determine the suitability of an antibody for diagnosis or treatment specifically in that patient.

Dr. TRIVELPIECE. Also last year, you had asked me about planning for the program. In connection with that, I had indicated that we were in the process of developing a 5-year plan. That plan was completed since the time of the last hearing. It is available now. It is called, A Plan for Biology Environmental Research Program. It is a bit long, and I don't know whether you would wish to have it incorporated into the record, but we would certainly be glad to make it available if you wish to use it for that purpose.

Also last year, just to clean up the slate, I had mentioned that it was my plan to empanel an advisory committee, the Health Environmental Research Advisory Committee, consisting of a collection of distinguished scientists and researchers in this field to advise the Department of Energy on the technical matters related to this program. I regret to say it has taken much longer to get this panel put together than I had anticipated. However, I am pleased to report that the first meeting of this committee will take place on March 19 of this year. I look forward to their trying to provide or providing for us the kind of guidance that we need in order to steer this program. I am sorry to say it has taken longer, but everything in government seems to take longer than you think it is going to before you start to do it. I haven't quite figured out how to fix that yet.

Mr. SCHEUER. When you do, let us know. [Laughter.]

Dr. TRIVELPIECE. One of the witnesses last week was Mike Phelps. You may be aware that he was the recipient of the Lawrence Award this year for his contribution to positron emission tomography. That is one of the things that has grown, in some sense, out of the Department of Energy's Health Environmental Research Program. In addition, there are two other individuals this year who will be the recipients of awards. One of these is Dr. John Lawrence. The other is Dr. Alex Hollaender.

Dr. Lawrence is the brother of E.O. Lawrence, the individual for whom the Lawrence Livermore and Lawrence Berkeley Laboratory is named. He literally is the father of nuclear medicine, and he will receive the Fermi Award this year for his contributions in that field.

Dr. Hollaender, who was for many years associated with the Oak Ridge National Laboratory, will be receiving the Fermi Award for his contribution as being essentially the father of radiation biology.

The ceremony at which those gentlemen will receive their awards this year will be on May 9. I would certainly like to take this opportunity to invite you, and other members of the committee if they could possibly attend, to be there. I think it will be an interesting event to really mark the very successful activities that the Department and its predecessor agencies, ERDA and AEC, have done in this particular field.

The nuclear medicine business involves now in the United States something on the order of 40 million people who receive 70 million nuclear medicine applications. I know one of the witnesses talked about this last week. This probably involves a business activity in excess of $10 billion. It certainly has paid off. If you were to ask whether or not it has been smart for the United States to have done this from a pure business sense, the answer is a clear yes. It

has also been an outstanding accomplishment in terms of the reduction in human suffering and the extension of human life.

The fact that it is good business still has to be taken into account in the present climate for research. As you know, the administration is strongly in favor of basic research and this year is trying to do something to improve our ability to train talent, to pick a few areas of research in which we will try to do things of excellence, and to establish a better partnership between our own laboratories and industry and universities. However, this has to be done in a climate in which there is a budgetary constraint. I have tried to maintain, in the constraining situation in which we have been operating, some of the core elements of the program. Before turning to questions, let me just mention one of the things that is kind of interesting that has come out of this kind of research program.

When you receive a cut, for whatever reason, there is a material, called a wound fluid, that appears in the wound. This fluid has the capability or some component of it, has the capability of causing capillarization to take place wherever you have been cut. That is a very essential feature, because without it, we wouldn't heal when we receive cuts.

One of the laboratories has been trying to isolate that particular component. The interest in this grows out of trying to understand the other side of this, that tumors and cancerous material have a capability of drawing to them a blood supply which they need for their existence and rapid growth. It is kind of an odd situation that it is two sides to the same coin, that this particular substance is absolutely essential for us to have wounds and things heal, and yet it is probably the same material, the same chemical substance that causes the rapid growth of cancerous substances.

So, trying to understand this chemistry and how it occurs and how to isolate it and so on is one of the elements. There are, of course, many other accomplishments, and I would be glad to talk about those.

Mr. Chairman, that completes the kind of introductory remarks I would like to make. I would be happy to answer any questions you might have.

[The prepared statement of Dr. Trivelpiece follows:]

Statement of Alvin W. Trivelpiece
Director
Office of Energy Research
Department of Energy
Before The
Subcommittee on Natural Resources, Agriculture
Research and Environment
House Committee on Science and Technology
March 13, 1984

Mr. Chairman and Members of the Subcommittee: I am pleased to have this opportunity to discuss the FY 1985 budget request for the Biological and Environmental Research (BER) program supported by the Office of Health and Environmental Research (OHER). This budget request reflects the goals and strategies set out in the Fourth National Energy Policy Plan (NEPP-IV), published in October 1983. As stated in NEPP-IV, the goal of our national energy policy is to foster an adequate supply of energy at reasonable costs. The strategies for achieving this goal are: (1) to minimize Federal control and involvement in energy markets while maintaining public health and safety and environmental quality, and (2) to promote a balanced and mixed energy resource system.

NEPP-IV recognizes that almost all energy production and consumption activities use or affect environmental resources - air, land and water--and that the benefits of such use should be balanced with environmental costs. One of the key ways for the Federal government to assure that the Nation's energy system remains environmentally sound is to support R&D programs aimed at analyzing the potential health and environmental consequences associated with energy technologies.

The BER program is the focal point of the Department's and Nation's efforts to acquire the scientific data required to anticipate, identify and

understand the long-term health and environmental consequences of energy use and development. This program takes an anticipatory rather than a regulatory approach toward the understanding of potential impacts on human health and the environment; that is, it tries to identify potential effects in advance and determine their magnitude, if any, at an early time so potential problems can be eliminated or controlled. This helps to avoid the imposition of costly corrective measures, such as retrofits or operating restrictions, at a later date.

BER program efforts are complemented by various technology programs in DOE and industry that primarily develop compliance oriented data on the relatively near-term impacts of specific energy processes. Various Federal agencies, including the Environmental Protection Agency, Nuclear Regulatory Commission and National Institutes of Health also support limited efforts on selected energy-related issues to meet their respective missions. Many interagency coordinating mechanisms are in place to provide forums for program planning and definition, research cooperation and information exchange. Internationally, we are developing closer working relationships with the Radiation Protection Programme of the Commission of the European Community (CEC) because the CEC is analyzing many important areas of interest to our programs.

The strength and uniqueness of the BER program can be measured in many ways: by the comprehensive and interdisciplinary approach for meeting its research objectives; by the recognition of the need to sustain a commitment to important long-term studies which are inherently costly and slow to yield significant results; by melding fundamental research to define how normal systems operate with applied studies to characterize how such systems are

affected by energy activities; by the development of a cadre of talented and experienced investigators and the specialized facilities and equipment necessary for conducting state-of-the-art science; and, of course, by the production of scientific data which reduce the health and environmental uncertainties associated with DOE's operations, policies and energy development programs.

Another measure of the strength of the program is the extent to which other agencies and DOE programs rely on BER facilities and scientists to meet their research needs. This year other sponsors are providing over $100 million to our laboratories to address problems of national significance. Such efforts complement the research performed for BER and often create a synergistic effect that benefits scientific productivity, operational efficiency and institutional viability. In fact, these outside funds have helped to provide for many of our facilities the stability necessary for effective operation.

The BER program also plays a role in the education and training of hundreds of graduate and postdoctoral students annually, provides collaborative opportunities for a comparable number of experienced visiting researchers, and shares the use of a host of unique instruments and facilities with hundreds of investigators from the research community. Nearly a third of the BER research is conducted on academic campuses and more than 200 scientists from our DOE facilities hold academic appointments, serving as an important resource in the formal education of the Nation's future scientists.

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I would now like to discuss the BER program proposed for FY 1985. In developing this budget request, the Office of Health and Environmental Research made a concerted effort to reevaluate the nature, scope and focus of our current program commitments while more clearly defining its future directions, rationale and priorities. A detailed account of our ongoing research efforts is presented in the publication "Research In Progress: FY 1984," (DOE/ER-0185, December 1983). A companion report entitled "A Plan for the Biological and Environmental Research Program FY 1985-1990" describes in some detail our vision and aspirations for the future. Copies of each have been provided to this Committee.

The BER program is not only long-term in nature but also broad in scope. It is important, therefore, to seek expert outside advice in the various areas of research emphasis. To obtain this assistance, a Health and Environmental Research Advisory Committee has been chartered. The expert advice obtained from the Committee will help us shape the strategic long-term planning necessary to establish research priorities for future budget years, determine proper program balance and identify opportunities for interagency cooperation and industrial participation. The first meeting of this Committee is scheduled for March 19-20, 1984.

The budget request for FY 1985 for the BER program (Table I) is $189.1 million, an increase of $5.2 million above the FY 1984 appropriation. Of this amount, $178.1 million is for Operating Expenses, $8.0 million is for Capital Equipment, and $3.0 million is for Construction. This budget request includes the CO_2 subprogram which is budgeted in the BER program but managed under the Basic Energy Sciences program. Funding by research area is shown in Table II.

Table I

Biological and Environmental Research
(B/A in Millions)

	FY 1984 Estimate	FY 1985 Request
Operating Expenses	$173.3	$178.1
Capital Equipment	8.3	8.0
Construction	2.4	3.0
TOTAL	$184.0	$189.1

Table II

Biological and Environmental Research
(B/A in Millions)

	FY 1984 Estimate	FY 1985 Request
Late Effects on Health & Environment of Energy Development & Use		
Source and Dose Determination	$ 10.2	$ 10.3
Environmental Fate & Behavior	28.3	32.7
Health Effects	62.7	57.3
Basic Biology	22.9	28.2
Risk Analysis	1.8	0
Nuclear Medicine	19.7	20.7
Carbon Dioxide Research	12.5	13.4
Program Direction	3.6	3.5
Facility Operations	22.3	23.0
TOTAL BER/OHER	$184.0	$189.1

The research area framework presentation shown in Table II differs from the disciplinary approach used in the past but is consistent with and ties to our five-year program plan to define more clearly the relative roles played by both our major research areas and special facilities in addressing BER program goals.

Let me summarize in the next few paragraphs the key research activities proposed for FY 1985 before proceeding to a more detailed discussion of each research area listed in Table II.

The primary goals for the BER program in FY 1985 will continue to focus on understanding the long-term health and environmental responses resulting from exposures to radiation and energy-related chemicals; and on the continued development of new stable and radioactive isotopes, labeled compounds, clinical procedures and visualization devices for improved diagnosis and treatment of human disease.

Overall, health-related research will be sustained at approximately FY 1984 levels, although a substantive refocusing of priorities is planned. Long-term human health and experimental animal research to quantify the long-term biological effects resulting from exposure to low levels of ionizing radiation will be continued. However, research on health and environmental effects involving nonnuclear energy options will decrease with the completion of short-term process-specific studies which helped define the classes of biologically active compounds warranting further study from among the thousands present in these complex mixtures. Much of the remaining research will address the uncertainties of carcinogenic, mutagenic, and toxicological effects of specific energy-related chemicals as well as

complex mixtures of chemicals. A substantial expanded effort is planned for basic biological research to define the mechanisms involved in the induction of biological damage following exposure to low levels of energy-related pollutants. This effort will be based on research related to biomolecular structure, gene function and control, genetic damage and repair, and cell transformation. The FY 1985 budget request does not include funds for the Risk Analysis subprogram. A number of risk analysis documents have been produced. They currently are being reviewed and will be completed in FY 1984.

Environmental research concerned with the transport, conversion and ecological effects of radionuclides and energy-related chemicals in water and on land will continue to define the processes by which radionuclides and energy-related materials cause damage to, and are cycled through aquatic and terrestrial systems. Research for characterizing the long-range transport and transformation processes of atmospheric pollutants will also continue; however, the high altitude sampling program to monitor the global behavior of radionuclides released by past nuclear testing activities will be terminated since the Department's original objective to document the level of radioactive debris in the upper atmosphere has largely been achieved.

A major field, laboratory and modeling investigation (which we expect to extend over approximately five years) to determine whether coal combustion source emissions are linearly or non-linearly related to acid deposition will be initiated and coordinated through the efforts of the Interagency Task Force on Acid Precipitation. The question of linear vs. nonlinear relationships turns on whether a given reduction in emissions from a source will result in a proportional reduction in rain acidity over ecologically

sensitive regions. This new initiative will complement our ongoing acid rain research program which includes studies of wet and dry deposition processes, development of models to describe transport and transformation of source emissions, and the maintenance of several research stations to sample rainfall in the eastern United States.

Research to improve our knowledge and understanding of the carbon dioxide issue will be expanded to determine whether trace gases like nitrous oxide, methane and freon may act like CO_2 in modifying climate.

The Nuclear Medicine program will continue to develop new isotopes and radiopharmaceuticals for advancing our understanding of human nutrition, cardiac function and neurological disorders.

Let me now summarize the BER budget request by research area.

Late Effects on Health and Environment of Energy Development and Use

The major objective of the BER program is to understand and reduce the uncertainties of potential long-term human health and environmental responses to chronic and acute exposures of radiation and energy-related chemicals. This uncertainty underlies all health and environmental issues associated with the Department's programs, policies and operations.

Quantifying the long-term biological effects in humans chronically exposed to relatively low doses of toxic materials is inherently difficult and requires long-term commitments. The availability of accurate dose estimates are limited and the biological effects are often small in magnitude, of relatively low frequency and difficult to attribute to a single cause. Yet a small increase in the relative incidence of a disease in human populations

or stress in an ecosystem may represent an unacceptable societal cost in absolute terms.

A. Source and Dose Determination

Estimation of health effects begins with a determination of the exposures received by humans or the environment. The FY 1985 budget request includes $10.3 million in Operating Expenses to support research to improve techniques to measure human exposure to ionizing radiation and to energy-related chemicals, to develop new measurement instrumentation and to define the physical and chemical nature of biologically active agents associated with energy technologies. These latter studies provide the input data required to understand how these agents move through the environment and to estimate human exposure to them.

For FY 1985, analytical studies will focus on characterizing the identity and biological potency of key chemical constituents within the complex organic mixtures previously found to be prevalent in most coal conversion process streams. In addition, research to understand how radon and radon-daughter concentrations vary for different building structures, ventilation rates, aerosol concentrations and other parameters will be continued and models developed for calculating energy deposition in the lung to better estimate the health risk of improved home weatherization measures.

Research on better ways to measure radiation doses, i.e., dosimetry, will continue to emphasize needs associated with human exposures. This will include dosimetry for mixed beta-gamma and neutron-gamma radiation fields, and improved dose definition to specific organs from internal and external radiation sources. Current investigations aimed at a complete reassessment

of radiation exposures received by the Japanese A-bomb survivors are approaching their conclusion. This multi-laboratory study was initiated when doubts arose as to the degree of neutron exposure, especially in Hiroshima. The study is of extreme importance for the reestablishment of cancer risk factors related to both human health data collected by the Radiation Effects Research Foundation in the estimation of radiation risks to man, and in the definition of standards for protection against radiation. Techniques for evaluating human exposure to biologically active energy-related chemical compounds will exploit developments in laser-based optical measurements to produce advanced personnel dosimeters and area monitoring systems with real time measurement capability for the workplace.

The development of innovative measurement concepts and novel measurement systems will also be pursued. This will include continuing fundamental research on the technology of semiconductor radiation detectors, detector materials and associated electronics, and on methods for low-level radioisotope measurements. Developments in picosecond lasers, ultraviolet lasers, multiphoton spectroscopy and other advances in photographic techniques will be advanced to permit the identification and quantification of specific substances within complex organic mixtures without time-consuming separations. Advanced instrumentation development for biomedical research will also proceed with emphasis on flow cytometers, optical and high resolution electron microscopy and position-sensitive detectors for use in biological structure studies and for measuring aerosol size and wet-dry depositions in atmospheric constituents.

B. Environmental Fate and Behavior

Once the source of a contaminant and its biologically active components

are identified, research is conducted to investigate the pathways and mechanisms by which these agents move through the environment, enter the food chain or other pathways to humans or affect critical ecosystems. The FY 1985 budget request includes $32.7 million in Operating Expenses for atmospheric, aquatic, and terrestrial research that will enhance our ability to determine exposures and potential impacts on human health and the environment.

For FY 1985, research in Atmospheric Science will continue to develop information required for improved understanding of the processes involved in the atmospheric transport, dispersion, chemical transformation, and deposition of airborne energy-related emissions as they move from source to receptor and for improving the capability for predicting the behavior and fate of such material. Current efforts aimed at defining atmospheric transport over complex terrain and regional-scale distances will be sustained. A highly successful series of experiments was conducted in FY 1983 and FY 1984 as part of the Cross Appalachian Tracer Experiment (CAPTEX) program. This program, which involves cooperation with the National Oceanic and Atmospheric Administration, the Environmental Protection Agency, and the Electric Power Research Institute, employed nonreactive perfluorocarbon tracers to develop and verify models of long-distance (approximately 1000 KM) transport and dispersion processes. This study will be concluded in FY 1985 with the final data analysis and publication of the report.

A significantly expanded effort is planned for ongoing studies dealing with the chemical and physical reactions of atmospheric gases and aerosols during transport. A new research initiative is designed to determine

whether there is a linear or nonlinear relationship between the processes by which SO_2 and NO_x are converted to acidic materials in clouds and removed by precipitation as "acid rain", i.e. to clarify the issue of whether a given reduction in source emissions will in fact result in a proportional reduction in acid deposition at given distances and times. The project involving laboratory, field, and modeling efforts by investigator groups from three of our laboratories will be closely coordinated with the research of other agencies through the Interagency Task Force on Acid Precipitation. The results of this research will help us further understand the complex acid rain issue.

Research on terrestrial and aquatic ecosystems has two major objectives. They are: (1) to identify physical, chemical, and biological processes that cycle materials through the environment and through food chains, and (2) to determine the resiliency of ecosystems to natural and induced stresses and identify processes used by plants and animals for degrading or detoxifying energy-related materials.

Research in cycling of natural and energy-related materials is conducted to identify and understand basic processes responsible for the chemical change and transport of both natural and energy-related emissions through terrestrial and aquatic ecosystems, to determine the rate of transfer of these materials through the ecosystems and into different food pathways, and to determine the final fate of these materials. Radionuclides, trace elements, and organic compounds from energy-related activities, as well as chemicals needed for ecosystems survival, are studied to determine how they are mobilized and moved through water bodies, soils, sediments, plants, and

animals. Coupling the research of energy-introduced substances with materials normally required by an ecosystem allows researchers to determine the critically needed information used in developing appropriate measures for redistribution and control of energy materials.

Studies of the biological responses of ecosystems are carried out using ecosystem structure, population dynamics, and physiological ecology to understand the resiliency of ecosystems exposed to natural stresses such as drought, fire, flood, etc. This knowledge on how well plants and animals accommodate to natural stresses is used to allow realistic estimates of the potential environmental impacts of energy development. Research is also carried out on metabolic processes which accumulate or eliminate metals from the ecosystem in order to determine more accurately those exposure levels that will allow ecosystems to exist without serious adverse impacts.

The cornerstone of long term terrestrial research in this program is conducted on land surrounding DOE facilities. Much of this land is protected for experimental research under the designation of the DOE National Environmental Research Parks. This network of outdoor environmental laboratories includes the major ecological regions of the U.S. Nearly every energy activity associated with fossil fuel, solar power, or nuclear systems is located on these or nearby sites. The availability of these controlled lands permits long term studies of ecosystem interaction with energy-related activities, providing effective strategies for the complete rehabilitation (and often enhancement) of sites disturbed by energy activities.

C. Health Effects

Health Effects research, for which $57.3 million in Operating Expenses is requested in FY 1985, is aimed at developing a solid base of knowledge to increase our understanding of human health risks that may result from exposure to ionizing radiation or to energy-related chemicals. Using some of the instrumentation developed in the Source and Dose Determination area, research is conducted on cancer, heritable defects and other delayed or late occurring health effects that may be associated with chronic exposures to low levels of radiation or energy-related chemicals. The effects of chronic, low level pollutant stress can be predicted only from extrapolation of effects from higher doses or from a scientific understanding of the underlying causes, basic mechanisms of damage and response, and normal functioning of unperturbed systems. The study of effects from chronic, low level exposures - those which are small in magnitude, occur infrequently, and are not usually attributable to a single cause - is difficult and requires a long-term research commitment. This comprehensive program of health effects research consists of interrelated studies of humans, animal species, and cellular molecular systems.

Research to better define the long-term effects of radiation exposure will be sustained at approximately the same level of support as in FY 1984. These include epidemiologic research on Japanese atom bomb survivors and radium dial painters, as well as health and mortality studies of over 700,000 workers who experienced occupational exposures at various nuclear shipyards, uranium mines, and DOE installations. Studies designed to provide quantitative data on the late effects produced in both short-lived and long-lived animal species exposed to radiation and radionuclides will be

maintained. Lifetime dog studies are producing data and relative cancer risks for the transuranium elements and selected fission products. Studies on radionuclide deposition and retention in organs are being conducted to determine critical organ dose and to clarify the basis for species differences in observed radiation-induced effects.

Neutron radiation biology will receive increased attention because data on human responses to neutrons, previously thought to be a major component of the total dose to which the Japanese populations were exposed in 1945, are now found to be lacking. As long-term animal studies are completed, research on the radiation effects at the cellular and molecular level, using human and other mammalian cells, will receive more emphasis. The objectives of this research are to clarify the mechanisms of radiation carcinogenesis, to define the role of DNA repair mechanisms in preventing or in mediating radiation-induced damage, to provide early indicators of delayed effects as well as exposure dose, and to better predict the health risks associated with radiation exposures at low doses and low dose rates.

Research on the long-term effects of energy-related chemicals will be refocused in FY 1985. Most of the effort will be oriented to evaluating the biological effect of complex chemical mixtures. Occupational studies currently underway for oil shale and coal gasification and liquefaction will continue, while studies involving the evaluation of the toxic potential of materials associated with renewable energy options and the short-term toxicity testing of synfuel mixtures will be greatly decreased. The potency of chemicals previously identified as potential carcinogens by cell testing will begin to be evaluated in rodents. Most of the other animal research will be devoted to more detailed studies in order to determine how

individual chemicals produce specific toxic effects in critical organs such as lung, skin, bone marrow and the immune system. The animal research also will investigate how combinations of chemicals in complex materials may interact to increase or reduce the effects of individual compounds of known potency. Included in this research will be studies on the metabolism, deposition, and retention of biologically significant chemicals (both organic and inorganic) in the whole animal and investigations of the genetic, reproductive and developmental effects produced by exposure to these energy-related chemicals.

D. Basic Biology

The Basic Biology research effort, for which $28.2 million in Operating Expenses is requested in FY 1985, is aimed at developing an understanding of the generic biological mechanisms which underlie human health effects of radiation and energy-related chemicals. To achieve this objective, research is carried out in structural biology, molecular biology and cell biology. To take advantage of new opportunities provided by recent advances in molecular and cellular biology and related fields, our basic research efforts will be refocused and substantially expanded in FY 1985. There will be decreased emphasis on studies in bacterial and other lower level biological systems (such as yeast) and additional resources will be applied to ongoing and new investigations using mammalian cells, with specific emphasis on human cellular systems.

There will also be increased emphasis on improving the basis for extrapolation of experimental data to humans and on the development of sensitive indicater systems for biological end points which can be directly

applied to humans. There will be increased use of unique DOE resources for biophysical studies of biological structure, for fundamental studies on the mammalian genes and for the important work of separation of human chromosomes. DNA from isolated chromosomes will be broken down to small pieces which are then replicated many times. These chromosomal-specific DNA pieces will be provided to the scientific community where they will lead to greatly increased knowledge of human gene structure, human genetic disease, and a variety of applications in both basic and clinical medical sciences. The strong program in DNA damage and repair will exploit recent advances to focus on a better understanding of human DNA repair capacity and its significance for human health.

Nuclear Medicine Applications

The development and application of nuclear techniques for diagnostic and therapeutic purposes has changed the practice of medicine by reducing the need for invasive procedures and exploratory surgery, making hospital stays shorter, less painful, and less dangerous. Our Nuclear Medicine Applications program, for which $22.1 million ($20.7 in Operating Expenses and $1.4 million in related facilities operations) is requested in FY 1985, has played an important role in these developments and continues to do so.

In FY 1985, the Nuclear Medicine Applications program will continue to provide new and improved sources of medically useful radioisotopes, new radiopharmaceutical agents, and improved instrumentation. It will also demonstrate the feasibility of these various applications in clinical medicine. Once feasibility is established, these new technologies, instruments, and isotopic materials are taken over by the private sector for

manufacture and distribution or by other agencies or institutions to be used for the study of specific diseases.

In addition to research on radionuclides for medical use, considerable work will continue to produce stable isotopes for use in biomedical research and medicine, to improve instrumentation for their detection and measurement and to evaluate the feasibility of using stable isotopes for new applications in medical research and diagnosis.

Research would also be supported to provide information necessary to evaluate the feasibility of using neutron capture techniques for the treatment of cancer; synchrotron light for improved diagnosis of coronary artery disease; heavy ions for the treatment of brain lesions; and shaped radiofrequency electromagnetic fields to treat cancer and abnormalities of the eye.

Within the Federal government this mission and DOE's facilities for conducting research in this area are unique. Liaison is maintained with Federal agencies (principally National Institutes of Health and Food and Drug Administration), the radiopharmaceutical industry, and the medical community regarding the requirements and the effective use of these techniques in medical research and practice.

Carbon Dioxide Research

The goal of the Carbon Dioxide Research subprogram, which is budgeted in the BER program but managed under the Basic Energy Sciences program, is to develop a sound, quantitative atmospheric carbon dioxide knowledge base to aid in energy policy decision making. We must improve our understanding of the fundamental scientific relationships between CO_2 concentration and

climate. This can only be accomplished by increased data collection, improved measurements, and development of reliable models.

The FY 1985 budget request of $13.4 million in Operating Expenses provides for completion of the State of the Art and Statement of Findings reports. These reports, scheduled for publication in early 1985, will delineate what is known, unknown, and uncertain about atmospheric CO_2, possible CO_2-induced climate changes and CO_2 vegetation effects. This effort will provide a better understanding about the long-term implications of CO_2 and will redefine the research necessary to provide a sound base for policy decisions.

In FY 1985, research into the effect of other trace (greenhouse) gases will be carried out. These gases, such as methane, freon and nitrous oxide, act similarly to CO_2 in affecting the return of radiation to space. Recent studies have indicated that these gases may have an effect ranging from half to equal that of CO_2's effect on the climate. Thus, in the analyses of climate effects from CO_2, these other gases must be included or a significant error could occur in our estimation of the magnitude and timing of a climate change.

Facility Operations

The national laboratories and other onsite specialized laboratories supported by the BER program represent an impressive national resource of skilled investigators, advanced major scientific instrumentation and exceptional, specialized research facilities. They provide the ability to address the diversity of research issues previously described while resulting in additional benefits to the scientific community at large.

But these facilities require a continued commitment to operate, equip, and maintain them. The FY 1985 request for Facility Operations is $23.0 million. Those funds will be allocated among the 18 laboratories which carry out much of the BER supported research. Of the total Operating Expenses request, $12.0 million is requested for utilizing a diversity of special resources, including cyclotrons and reactors, environmental research parks and measurement laboratories as well as advanced spectrometers, electron microscopes, synchrotron light sources, and flow cytometers.

A Capital Equipment request of $8.0 million is required for pursuing the diverse areas of research, to maintain state-of-the-art capability for ongoing research and for equipment to initiate new research efforts, and to replace older instruments whose continued use and operation is no longer cost effective. Examples of equipment needs include scanning electron microscopes, liquid chromatographs, liquid scintillation counters, spectrometers, amino acid analyzers, environmental chambers, infrared analyzers, etc.

The FY 1985 Construction request of $3.0 million is required to support the programs General Plant Project needs including the Pacific Northwest Laboratory landlord responsibility. These General Plant Projects will provide facilities for conducting critical research programs, contribute to greater efficiency, eliminate health and safety hazards, and will reduce maintenance and operational costs.

Mr. Chairman, that concludes my testimony. I will be pleased to respond to questions.

U.S. Department of Energy
Assistant Secretary for
Congressional, Intergovernmental
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Washington, D.C. 20585
202/252-5644

BIOGRAPHY

ALVIN W. TRIVELPIECE

Dr. Alvin W. Trivelpiece was nominated by the President on July 8, 1981; and confirmed by the Senate on July 27, 1981, as Director of the Office of Energy Research, U.S. Department of Energy (DOE). In this position, Dr. Trivelpiece serves as technical adviser to the Secretary on the Department's energy research and development programs and is responsible for the multipurpose laboratories and energy education and training activities. In addition, he manages DOE's programs for basic energy research, health and environmental research, high energy and nuclear physics, and magnetic fusion.

Dr. Trivelpiece has extensive experience in the areas of plasma physics and fusion research. From 1978 until assuming his current position, Dr. Trivelpiece was Corporate Vice President of Science Applications, Inc., of La Jolla, California, primarily responsible for internal research programs relative to innovative technical developments. From 1976 to 1978, he was Vice President for Engineering and Research at Maxwell Laboratories, San Diego California.

During the period 1973 to 1975, Dr. Trivelpiece served with the U.S. Atomic Energy Commission as Assistant Director for Research in the Division of Controlled Thermonuclear Research. Prior to joining the Federal Government, he was Professor of Physics at the University of Maryland, serving in that capacity from 1966 to 1976. From 1959 to 1966, he was a professor at the University of California at Berkeley in the Department of Electrical Engineering.

He received a B.S. degree from California Polytechnic State University in 1953, an M.S. degree in 1955, and a Ph.D. degree in 1958. Both advanced degrees were awarded by the California Institute of Technology.

The recipient of several honors and awards, Dr. Trivelpiece is listed in American Men and Women of Science, Who's Who in America, and Who's Who in the World. He holds several patents in the area of physics research and is the author and coauthor of over 100 technical reports and books.
Dr. Trivelpiece is a member of numerous professional organizations and is a fellow of the American Physical Society, the Institute of Electronics and Electrical Engineers, and the American Association for the Advancement of Sciences. He has served as a consultant to various private associations and Government agencies and has lectured at conferences and universities throughout the United States and abroad.

Dr. Trivelpiece was born in Stockton, California. He is married and has three children.

June 1983

Mr. SCHEUER. Thank you very much, Dr. Trivelpiece. I have a couple of questions, and then I will recognize my colleagues.

The laboratory at UCLA is engaged in a cancer research project in nuclear medicine, Alzheimer's disease, and cardiovascular disease. DOE funding for this program has been, up to now, at a level of about $4 million annually. However, your fiscal year 1985 budget cuts the request of this lab to zero.

Now, we had a hearing on March 6, and witnesses testified at that hearing that the quality of research at the UCLA lab is equal to that conducted anywhere in the world. What is the reason for terminating that contract?

Dr. TRIVELPIECE. I think there has been a slight misunderstanding which is a semantic difficulty. That is, there is a difference between terminating a program and terminating a contract. In the attempt to try within—to live within the budget guidance we had been assigned, we looked for mechanisms by which we might save some money. Several contracts were examined with the possibility of revising the mode by which the activities were funded in order to save money.

As it turns out, the subsequent analysis of the terms and conditions under which those contracts were created reveals that the kinds of savings which we thought might be available are probably not there. I am reexamining that. I think the chances with UCLA are that the program would continue more or less as is. Some of the others, the chances are that some of those would be reduced for programmatic reasons, but there is a distinction to be drawn between terminating a program and terminating a contract. There was no intention of terminating the program. There was an intention of modifying the mode by which the work was funded. That misunderstanding has been somewhat unfortunate.

Mr. SCHEUER. Well, would you keep in touch with us and let us know what happens to that particularly program?

Dr. TRIVELPIECE. Certainly.

Mr. SCHEUER. One of the goals of DOE research is, and I quote, "to develop new applications of nuclear science and technology for use in the diagnosis and treatment of human disease." It seems to me that this UCLA lab research program directly addresses this goal.

Dr. TRIVELPIECE. No dispute.

Mr. SCHEUER. No dispute. So, the village is worth saving without destroying it? Do you remember that famous quote by one of our generals during the Vietnam war? That we had to destroy the village in order to save it? You wouldn't apply that reasoning to this program, would you?

Dr. TRIVELPIECE. I certainly hope not.

Mr. SCHEUER. OK. Will you let us know?

Dr. TRIVELPIECE. I would be delighted.

Mr. SCHEUER. Thank you.

Apparently, after the Office of Management and Budget examined the DOE budget request for fiscal year 1985, several program suggestions were made. One of them I would like to have you explain to me, elucidate a little. I find it very puzzling. One of the comments they made was, "No new epidemiological studies should

be initiated unless DOE can demonstrate in advance that the results will be statistically significant."

Dr. TRIVELPIECE. I think that is a fair admonition to be made in almost any circumstance whether it comes from OMB or anyone that, in order to have accurate and useful information from an epidemiological study, it is necessary that the population be large enough that the thing that you are trying to study in connection with that be capable of being resolved statistically. It doesn't say not to do epidemiological studies. It just says don't do any careless ones and don't do any for which the possibility of getting relevant information is not going to be available.

In that regard, one of the first charges that I am going to make to the Advisory Committee that is empaneled is to ask them to look into the present epidemiological studies and to report back to me on those that are currently going on and those that might be useful in the future.

Mr. SCHEUER. This quote that I have just given you suggests to me, at least, that before a research program can be started, the final results must be known. If they have to prove in advance that the results will be statistically significant, you are saying you have to know the results before you do the experiment.

Dr. TRIVELPIECE. I am not sure of the exact origin of OMB's concern. I am trying to interpret what I believe their statement would mean. If you were to try to do a cancer survey on, say, 10 people, the chances of obtaining statistically relevant information would be rather small. It takes a very large sample to do so.

Mr. SCHEUER. Suppose you wanted to do a cancer survey on 1,000 or 10,000 people. There is no questions that that would be an adequate sample, as to whether rice pudding or chocolate ice cream with fudge sauce was a better diet for cancer. Does that statement mean that you simply have to have a large enough sample for the result to be statistically significant, or does it mean that you have to compute in advance what the result is going to be, that it is going to tell you whether rice pudding or chocolate ice cream with fudge sauce is going to be a better diet?

Dr. TRIVELPIECE. Certainly, a large enough sample is an essential condition for proceeding.

Mr. SCHEUER. Agreed. How about the result? Must the result be known before you engage in the research?

Dr. TRIVELPIECE. No; but there should be some reasonable expectation that you can get a result from that population. There are statistical tests that you can apply to determine whether or not the cost of a full study would be warranted.

I don't think they are saying anything that is not good scientific practice in that statement. It isn't clear that it has any direct budgetary consequences in that there is not a particular dollar sum associated with that activity.

Mr. SCHEUER. It looks very much as if they are saying you had better know what the research—you had better be able to demonstrate what the research is going to prove before you do it. If it does mean that, that is a very sad commentary. Where would scientific research be, going back hundreds or thousands of years, if before Newton dropped the apple from the leaning tower of Pisa, he had to prove what it was going to prove about gravitational

forces. Scientific research is always a probing into the unknown. Sometimes we learn something and sometimes we don't.

If you are going to limit all scientific research to where you can predict with clear certainty the results of the research, you have irremediably wounded the scientific process, it seems to me.

Dr. TRIVELPIECE. I took it in the spirit of being a helpful admonition and an admonition to do the science in which we are engaged in a proper manner and not as being something that prohibited in any way an epidemiological study that was of importance to the Government.

Mr. MOLINARI. Would the chairman yield?

Mr. SCHEUER. Sure.

Mr. MOLINARI. I have to leave, but I would love to ask one question on this subject.

Mr. SCHEUER. By all means.

Mr. MOLINARI. I think perhaps to understand better what you are saying and what OMB is saying, can you give us some examples of studies that have been conducted in the past that fit into the category described here where the results were not statistically significant? What are they trying to eliminate? Have there been some programs? Can you give us some examples of the kind that are described or intended to be described here?

Dr. TRIVELPIECE. I suppose probably smoking is a good example in that there was an early period in which there was a great deal of debate on whether or not the results being obtained were statistically relevant. However, as years have gone by and additional data has been available, the correlation, as published by the Surgeon General indicates that there is a clear correlation between certain health hazards and personal smoking.

To some extent, even those statistical results are still debated and aspersions cast on their validity by certain individuals.

Mr. MOLINARI. If the gentleman will permit one further question, I had assumed that it was something more recent that they were referring to here, something in the last year or two. Otherwise, I don't know why they would have included this statement. Is there anything of more recent vintage that you know of?

Dr. TRIVELPIECE. OMB did not communicate with me about any particular statistical study for which they were concerned, for which that remark was made.

Mr. SCHEUER. There are no horror stories lurking back there in recent history?

Dr. TRIVELPIECE. I don't know. Perhaps Dr. Edington knows of some, but I don't know of any.

Dr. EDINGTON. Mr. Chairman, I think what OMB was trying to relate to us was that before any epidemiological study was initiated, that we should take a look at the size of the population, the exposure level either to a chemical or to radiation, and the probable level of effect that might be produced per unit dose which would allow you to determine the population size needed in order to demonstrate a significant difference before you initiate that experiment.

I can give one example. We were asked at one time to conduct a genetic study to measure the increase in human mutation rate. We had only the mutation rate in mice at that particular time, so that

we knew that the mutation rate was low per gene locus, per unit dose. We calculated that, in order to show a 95 percent level of confidence that there was a statistically significant difference would require 10 billion mice.

That is a mind boggling number. There is no way that one could do an experiment with 10 billion mice to demonstrate a significant difference. Therefore, in our opinion, the feasibility of doing that study was not there. We didn't have the tools, we didn't have the facilities, and we didn't have the people to do that.

I think that is probably what they were trying to say to us. We are smart enough, I think, to know that we would not use taxpayers' money to initiate a study that would not allow us to demonstrate some kind of an effect.

Mr. SCHEUER. They were really telling you to be sensible.

Dr. EDINGTON. I think they may have been telling us to do that.

Mr. MOLINARI. Continue your present practice is what they were saying.

Dr. EDINGTON. That is what we would intend to do.

Mr. MOLINARI. Thank you very much, Mr. Chairman.

Mr. SCHEUER. Thank you, Leo.

It seems to me that just taking the example you used, the tobacco studies over 20 years, they have been criticized over the years by the Tobacco Institute as not being statistically definitive, not that the results were not statistically significant, but they were not statistically definitive. Well, you can't put a large group of people into a laboratory. The results always have to be subject to interpretation. However, there has been a drumbeat of criticism by the Tobacco Institute over the years that these studies were not valid. I think now after 20 years of study after study after study has shown an alarming degree of statistical relevance in the relationship between smoking and cancer as well as between smoking and a lot of other serious ailments, heart failure, stroke, and many other illnesses, that there is an overwhelming consensus in the medical profession that smoking is bad for you in a wide variety of ways.

Would this criterion, that the results have to be statistically significant, have cut off this cancer research in the early years before the consensus finally emerged with virtual unanimity among responsible leaders in the medical profession?

Dr. TRIVELPIECE. I don't think so.

Mr. SCHEUER. They weren't saying anything more than be sensible?

Dr. TRIVELPIECE. That is my interpretation, and absent further guidance, I am going to stick to it.

Mr. SCHEUER. OK.

Dr. EDINGTON. Mr. Chairman, may I add one comment?

Mr. SCHEUER. Yes, of course.

Dr. EDINGTON. There is a situation in which one does this calculation ahead of time to determine whether or not all the parameters of the study are there to allow you to measure something significantly. When you deal with low level radiation or chemical exposures, you have a problem because the doses are so low, the mutation rate or the cancer rate is so low, that it would take a very, very large population in order to show a statistically significant difference between the exposed and the control.

However, one can with that same population, if it is sufficiently important, get data which would allow you to establish an upper limit of what the effect might be at a very low dose level. That would be the best measure that you might be able to get in a human population of radiation exposure or chemical exposure. Therefore, that would be compared to what you see at a very high radiation exposure where you have to extrapolate down into that low level area. On occasion we do studies of that type which would allow us to get the upper estimate of a low level effect.

Mr. SCHEUER. Thank you.

Congresswoman Schneider?

Mrs. SCHNEIDER. Thank you.

Dr. Trivelpiece, it was also mentioned in this same OMB response that what you should do is close out technology specific research and focus more on long-term generic research. I wonder if you could be specific as to what they are talking about?

Dr. TRIVELPIECE. The activities associated with, say, production of synfuels, there were a variety of different processes. One company proposed one way to do it and another company proposed another way to do it. In each case, some quantity of a synfuel was produced. Then, the question was, should you study independently the toxicity, mutagenicity, carcinogenicity of each of those particular products from that particular process, or should you take a look at the generic characteristics of hydrocarbons no matter where they are produced and what toxicity they might have in various forms.

Mrs. SCHNEIDER. To me that seems like the obvious way to be doing the research. Does that mean to say that DOE had not been doing that approach in the past?

Dr. TRIVELPIECE. That is correct. Previously there had been process specific activities being done at several laboratories. One of the results of that was a recognition of the fact that there are some very common subsets of the hydrocarbon populations in these that are responsible for the bad effects, the toxicity, and, can in fact, be reduced or hydrogenated out of the process stream.

So, the trend has been to get away from those technology specific activities into generic activities to understand the toxicity of chemicals.

Mrs. SCHNEIDER. Could you supply us with a list of those technology specific projects that are now going to be translated into the generic approach and supply that to us for the record?

Dr. TRIVELPIECE. Certainly. I would be delighted to do so.

Mrs. SCHNEIDER. Thank you.

Mr. SCHEUER. Perhaps with some explanation of what will be involved in that transfer.

Dr. TRIVELPIECE. Yes.

[Material referred to follows:]

TKANSITION OF TECHNOLOGY SPECIFIC PROJECTS

Between 1976 and 1982 the Office of Health and Environmental Research (OHER) sponsored a series of integrated research efforts to characterize the health and environmental acceptability of advanced fossil fuel technology options, including coal liquefaction, coal gasification, shale oil, and fluidized bed combustion. The investigations were conducted at Argonne National Laboratory, Los Alamos National Laboratory, Oak Ridge National Laboratory, Pacific Northwest Laboratory, and Lovelace Inhalation Toxicology Research Institute. Many of these research efforts were conducted in collaboration with the Office of Fossil Energy as well as the private energy sector. A diversity of promising energy processes, at stages of development ranging from bench scale, pilot plant to commercial scale were evaluated to provide a perspective of how much the chemical, physical and biological characteristics of the different process stream constituents varied. For the most part, this phase of research addressed short-term issues, and data was obtained which provided a base for addressing the long-term health and environmental questions underlying the establishment of a synthetic fuels industry. This phase of work is now complete. A series of status reports have been prepared by the laboratories documenting their results for coal liquefaction, coal gasification, coal combustion and solid wastes from such processes, as well as a risk analysis report on the health and environmental effects of the shale oil industry. A synthesis of these efforts was also performed as part of a workshop series to crystalize conclusions regarding our current understanding of the field, identify existing data gaps and develop recommendations[5] for the future research priorities. The proceedings of these deliberations have been published and widely distributed. These efforts have provided the OHER staff with a basis for developing a research plan (phase II) which addresses long-term, generic, health and environmental issues related to synthetic fuel processes. The proposed research has been described in the OHER five year plan (A Plan for the Biological and Environmental Research Program FY 1985-1990), and in greater detail in "A Research Plan for Resolving Problems in Evaluating the Health and Environmental Effects of Complex Chemical Mixtures[5]," which is currently in draft. Both of these documents are to be reviewed in detail by the Health and Environmental Research Advisory Committee. The focus of the phase II effort for synthetic fuels-related health and environmental research is to understand how and why the biological activity of complex mixtures, typical of synfuel process streams, are different qualitatively and quantitatively from the activity observed when the individual components of the mixture are investigated alone. Unless resolved, regulations based solely on concentrations of individual components cannot in themselves be used to predict the biological activity of synthetic fuels or other complex mixtures. The cadre of scientists who participated so successfully in the phase I effort will, to a large extent, implement the projects proposed for phase II.

Mrs. SCHNEIDER. I wonder if you could elaborate on the fact the fact that there are no funds for indoor air quality research?

Dr. TRIVELPIECE. I am not sure what you mean by indoor air quality research. We think there are some funds in there, and that is the measurement to try to understand where the radon comes from, and how it gets into buildings and how it is trapped. Could you be a little bit more specific in your question?

Mrs. SCHNEIDER. DOE is supposed to be coordinating activities with EPA on not only radon but other types of indoor air pollution. The outcome of this joint study on indoor air quality is supposed to be compiled and reported back to Congress.

Dr. TRIVELPIECE. Two things. We do the work on the measurements and we also do work on trying to understand the tumor potential for radon daughter products and so on. That work has been going on at Pacific Northwest Laboratories. We are doing both. It is not zeroed out.

Mrs. SCHNEIDER. It is not zeroed out? Let me just make sure that I understand what we are looking for in these studies. No. 1, measurements and identification of different pollutants. Is that what DOE is going to be doing?

Dr. TRIVELPIECE. We have been doing it primarily with radon. I am not aware of others.

Dr. EDINGTON. In our indoor air research activities, we are looking at radon and radon daughter products from concentrations and effects, but we are also looking at only two other products. One is formaldehyde which comes out of pressed wood, things of this type, furniture, et cetera, and also at some of the synthetic insulation materials, glass fiber, glass wool, things of this type. However, not asbestos.

We are involved in an interagency indoor air task group with EPA about 10 or 12 other agencies. We are not necessarily involved in just monitoring. We are more concerned about the source, the transport of the material in the indoor environment, and the effects. We basically concentrate on radon because no other Federal agency is involved in that particular type of activity.

Mrs. SCHNEIDER. What kind of acitvity are you planning for 1985 as it might relate to radon or any other biological effects of indoor air pollution?

Dr. EDINGTON. We will continue the current study at approximately the same level. It is at a level of about $1.5 million in which we will be looking at the transport mechanisms, the distribution of radon in the indoor environment, and we will be looking at the effects of radon and radon daughters on lung tumors where basically one would find the biological effects.

Mrs. SCHNEIDER. But once again, that $1.5 is strictly confined to radon and radon daughters.

Dr. EDINGTON. Formaldehyde and insulation products.

Mrs. SCHNEIDER. It does include formaldehyde?

Dr. EDINGTON. They are all three included in the $1.5 million.

Mrs. SCHNEIDER. OK.

I also wanted to ask you about the proposed 41 percent addition to the nuclear safety program. What kind of specifics are you planning there?

Dr. TRIVELPIECE. I think Dr. Jan Mares, Assistant Secretary for Environmental Health and Safety, would be better prepared to answer that question since it is in his budget.

Mrs. SCHNEIDER. All right. We will save that one until later, then.

What about risk analysis? No funds are being provided for risk analysis?

Dr. TRIVELPIECE. That is the activity which when we looked at the priorities within the constrained budget guidance that we were working, was at our lower priority limit. It involves interpretive results of the experimental activities that are done. It is my view that protecting the laboratory and experimental activities is more important than protecting the risk analysis.

Mrs. SCHNEIDER. What is the value of the various laboratories doing the research if we are not in a position to do the interpretive work that is necessary?

Dr. TRIVELPIECE. Well, in part, we are assuming that the Environmental Protection Agency, which is in a better position in some cases to do these risk analyses and risk assessments and risk management studies, will be in a position to take the data we generate from our laboratory and scientific studies and utilize it for that purpose.

Mrs. SCHNEIDER. I don't think they will be in a position where they could translate the biological data into epidemiolgical impacts. I would think that they would not be equipped, given their limited research into biological effects, I wouldn't think that they would be equipped to interpret them.

Dr. TRIVELPIECE. My understanding was I thought they were supposed to be able to do that kind of thing.

Mrs. SCHNEIDER. That is something that I am going to have to ask EPA about too, because it seems like they are pointing to you and you are pointing to them. In essence, nobody is looking at what value risk assessment and risk analysis has. To me, there is no point in doing research unless we translate the findings and say what the impact of various pollutants or various activities are.

Dr. TRIVELPIECE. I am not trying to say there is anything wrong with this work. It is that this was that project which, given the constraints under which we were operating, we felt was lowest priority within the activities that we were managing.

Mrs. SCHNEIDER. And I guess what I am saying is that if I were in a similar situation, I am sure that I could find some areas where we could shift the moneys and put them into risk analysis because, from my point of view, all the other dollars being expended on research are worthless unless we can interpret them and to share with the general public the risk that they are being exposed to based on the scientific data that we have accumulated.

I will pursue this with EPA and see if we can get some kind of coordinated response on this. To me, budgetary constraint does not seem an appropriate justification for its elimination, especially when it is so closely tied into the other basic research that you folks are involved in.

I have no further questions, Mr. Chairman. I thank you, Dr. Trivelpiece.

Mr. SCHEUER. Thank you.

Mr. MacKay?

Mr. MACKAY. Doctor, I am trying to get some basic background information so that I can understand how your program coordinates with EPA and NIH research and Food and Drug Administration research.

I see that you mention that there are many interagency coordinating mechanisms in place. It seems to me that our present administration has a policy that basically says we are going to rely on fossil energy and nuclear fuel particularly, and we have deemphasized the research on alternative sources, solar energy and that kind of thing.

Dr. TRIVELPIECE. I would disagree with that statement based on the Secretary's posture and statements before this committee and the full committee. He has been trying to state clearly that what we need is an adequate supply at a reasonable cost and that one of the things that that entails is having a balanced mix of energy resources. Certainly it is true that nuclear and coal and oil for the near-term are going to be what we are going to have to use, but he has made an effort to ask for—and I don't have the details in my mind on the budget levels that have been requested for alternate energy sources—but the Department's program now includes those as an element.

Mr. MACKAY. In terms of the basic budget allocations in this administration, say, as compared to the previous administration, it would appear that the emphasis on alternative energy sources is substantially less.

Dr. TRIVELPIECE. They are down. That is clear. The trend is up. That is also clear, in the last year. I would be glad to supply the other elements of the Department's budget for you if you would like those in the nonfossil, nonnuclear areas.

Mr. MACKAY. My point would be that with the difference in emphasis, regardless of the trend, we would find a greater need for research on acid rain and radiation and the, in effect, health and environmental consequences of continuing on the course on which we find ourselves. Your testimony said we are trying to get into an anticipatory rather than a regulatory.

Dr. TRIVELPIECE. The administration's budget for acid rain has been doubled this year.

Mr. MACKAY. I understand that. That is like saying the trend is up. Do you see that we are in a mode where you can properly characterize our efforts as anticipatory in the acid rain area?

Dr. TRIVELPIECE. I am one of those that subscribes to the proposition that we need to know a great deal more about acid rain before putting in place any mitigation strategy. I am certainly not unhappy about the increase in acid rain research that the administration has requested. Whether or not that will, in a very short time, answer all the questions, I think remains to be seen.

The kinds of research that I perceive as being necessary are beginning, and this includes the control technology aspects of the Department's budget as well as some of the things in the EPA budget for the lime injection multistage burners as weil as basic research in this program which involves the nonlinearity of acid rain as well as the Captex experiment and various others. I think those are all

important pieces of research to be done in order to acquire the data necessary to determine what the cause and effect relationships are.

Mr. MACKAY. Would you say, since you are the Department of Energy and it seems that acid rain may be related to the production or the consumption of energy, is it primarily your agency's responsibility to provide us the knowledge in this area?

Dr. TRIVELPIECE. No. The Congress created an interagency task force on acid precipitation, and DOE is not one of the lead agencies. It is Agriculture, EPA, and NOAA, I believe. They are the three leading agencies. We participate in that task force and we are doing part of the work and coordinating with the activities recommended by the task force.

Mr. MACKAY. If I were then to ask you in your own words to say where do you have the primary responsibility in this question of environment and health research, would you give me a brief kind of narrative on that?

Dr. TRIVELPIECE. Sir, could you repeat the question please?

Mr. MACKAY. Yes; where do you have the primary responsibility as the Department of Energy for the research effort on the health consequences of the uses of energy?

Dr. TRIVELPIECE. Certainly in the area of radiation, and this goes back to the Atomic Energy Act in which the risks associated with various radionuclides is to be understood as well as the potential benefits that might be derived from them and radiation. Certainly that is an area in which the Department has exclusive responsibility. I am not sure of the exact date, but sometime in the early 1970's in addition to responsibility for radiation, additional responsibilities were taken on by the Department for various chemical agents related to the energy producing activities.

As far as I know, the Department is the only national agency that has responsibility for trying to understand the toxicity and other human health effects associated with energy producing chemicals and effluents.

Mr. MACKAY. In the CO_2, the greenhouse effect research, is that your primary responsibility?

Dr. TRIVELPIECE. The budget for that is carried in this program. However, the management is carried out under another program called Basic Energy Sciences. That is about $13 million. That represents, I think, about half of the present U.S. research in CO_2. There is an interagency task force on CO_2. DOE is the lead agency for that. We do coordinate our activities with the other agencies.

Mr. MACKAY. All right. Thank you.

Thank you, Mr. Chairman.

Mr. SCHEUER. Do you have anything further, Mrs. Schneider?

Mrs. SCHNEIDER. No, thank you, Mr. Chairman.

Mr. SCHEUER. We may have some more questions that we will submit to you in writing for the record, and we will hold the record open for another 10 days or 2 weeks.

Thank you very much, Dr. Trivelpiece, for your testimony.

Dr. TRIVELPIECE. Thank you, Mr. Chairman.

Mr. SCHEUER. Next we will hear from Mr. Jan Mares, Assistant Secretary for Policy, Safety, and Environment, Department of Energy. He is accompanied by Robert W. Davies.

Mr. Mares, your prepared testimony will be printed in full in the record. What we suggest is that you chat with us informally for 5 minutes or so, and then I am sure we will have some questions for you.

STATEMENT OF JAN W. MARES, ASSISTANT SECRETARY FOR POLICY, SAFETY, AND ENVIRONMENT, U.S. DEPARTMENT OF ENERGY; ACCOMPANIED BY ROBERT W. DAVIES

Mr. MARES. I would be pleased to do that. I want to first say that I testified yesterday before the Senate Subcommittee on Energy Research and Development about acid rain, about the Federal research program and put it in the context of policy and environmental issues and I would like to attach that to my testimony because I think it is responsive to many of the questions that Congressman MacKay was asking.

A copy of the statement of Jan W. Mares, Assistant Secretary for Policy, Safety, and Environment, before the Subcommittee on Energy Research and Development, Committee on Energy and Natural Resources, on March 12, 1984, is attached for the record.

Mr. SCHEUER. Excellent.

Mr. MARES. I might even answer one of his questions that he asked about——

Mr. SCHEUER. I wish you would because we are all interested in his questions. This whole business of the Government, the administration taking the position that we have to know everything about acid rain before we can do anything, to us, is utterly frustrating and very disappointing.

Mr. MARES. I think that is not a fair characterization of the administration's position, but let me first address one major question he asked which was, what was the Department's role.

One of the very important roles the Department has, as it relates to acid rain, is the request for about $55 million to develop technologies that would allow us to remove sulfur and ash from coal before it is burned, to burn coal more efficiently and in ways that do reduce the amount of SO_X and NO_X, and finally to remove SO_X and NO_X from the effluent gases. Those programs are carried by the Office of Fossil Energy, and they have testified before this committee, a different subcommittee, but part of this committee.

Mr. SCHEUER. Just for the record, will you clarify SO_X and NO_X.

Mr. MARES. SO_X is sulfur oxides, could be sulfur dioxide or sulfur trioxide. NO_X are the oxides of nitrogen which could be NO_2 , NO_3, and a whole series of oxides. It is shorthand that is used—I am glad you asked the question. My wife asked me the same question yesterday and I had to explain it to her, so I should have been more precise.

If I may, I would like to summarize my statement regarding the budget that we are requesting here briefly. You know the Department is committed to having its activities operated in a safe, healthy, and environmentally sound manner. Our headquarters office is charged with establishing policy, providing guidance to the Department on these matters, as well as providing an independent overview of the assessment capabilities to the Secretary and the senior management.

We have had an outstanding safety record in 1983, and expect to continue that. I would draw your attention to the charts that are on pages 14 through to the end of my testimony which indicate, by almost any comparison, that the Department's health and safety record has been outstanding compared to both the previous performance of the Department, as well as public and private sector experience, to the extent that we have standards available to compare against.

None of our 1983 injuries or illnesses were caused by radiation exposure and there were no accidental exposures in excess of various allowable annual limits.

With respect to our budget, we are requesting a budget of $37 million which is about $5 million more than we requested or was appropriated for 1984. This increase——

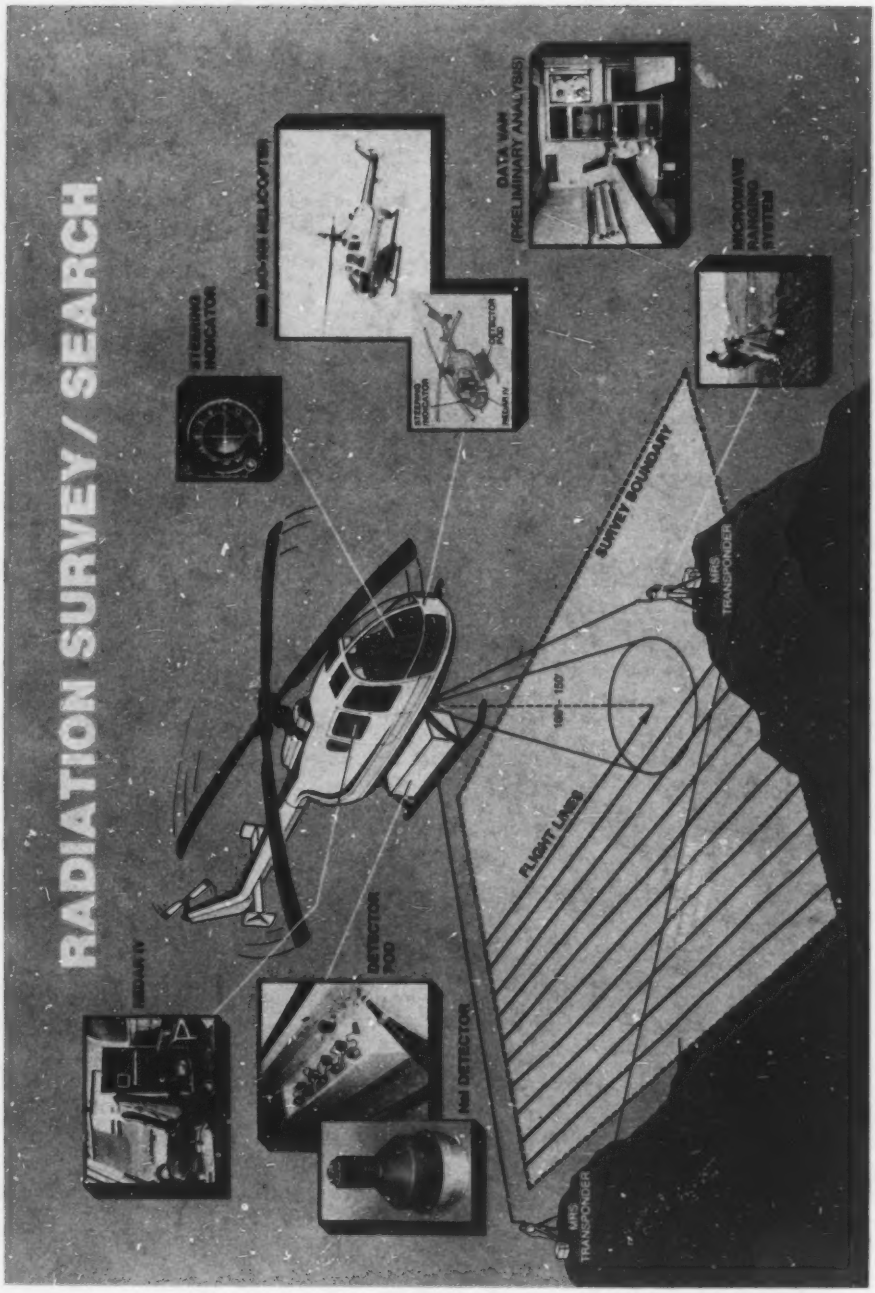
Mr. SCHEUER. With the witness' permission, my colleague has a question for you.

Mrs. SCHNEIDER. Mr. Chairman, I can withhold my question until he has completed his statement.

Mr. MARES. Well, one of the questions you asked earlier I can answer for you right now, that is, this increase is primarily in the nuclear safety area. It is a substantial increase by percentage terms, even by absolute terms. We are convinced it can be spent intelligently. I have a detail of each additional project that we are seeking funds for. Most of them are going to be done by the national labs or other contractors, would not require a change in the personnel staffing of our office, and we think that each of the pieces stands on its own, can be managed on its own by us in an intelligent fashion even though the totality, when added, shows a substantial increase.

One of the things that increase deals with is that it would allow us to enhance our remote sensing capabilities of our aerial measurement system. That is the significance of these charts that we have over here. I wanted to talk about it briefly because this is a significant capability that the Department has and it is being used right now in Mexico.

[Charts referred to follow:]


RADIATION SURVEY / SEARCH
HIDAR IV
DETECTOR POD
NaI DETECTOR
STEERING INDICATOR
DATA VAN (PRELIMINARY ANALYSIS)
MICROWAVE RANGING SYSTEM
SURVEY BOUNDARY
FLIGHT LINES
MRS TRANSPONDER
MRS TRANSPONDER

36-326 O - 84 - 14

AIR CARGO
POD SYSTEMS
PHOTO
VIDEO
MECHANICAL
GENERATOR
COMMUNICATIONS

DATA ANALYSIS
CONTOUR PLOTTER
GAMMA RADIATION ANALYZER LABORATORY
MOBILE RADIATION ANALYSIS LABORATORY
PORTABLE GAMMA RADIATION ANALYZER SYSTEM
FLIGHT LINES
MAN-MADE RADIATION CONTOUR
SPECIFIC ISOTOPE CONTOUR
GROSS RADIATION CONTOUR
TYPICAL LINE PLOTS
TYPICAL GAMMA SPECTRA

Mr. MARES. As you may know, a cobalt 60 medical source was sent to a Mexican facility. They did not use it. It was sent to a junk yard, broken into in the junk yard. Radioactive particles of cobalt 60, which are about the size of a penny, and I think the staff director has a picture of those particles, several thousand of them in one of these sources. They were spewed out in the junkyard as well, as the source, with some of them were sent to a foundry which then made reinforcing bars which came into our country. It has been detected in various places. There is no public health concern about the use of the reinforcing bar or some table bases containing metal, which does have some of this cobalt 60 in it.

We were asked by the States of Texas and New Mexico to survey to determine whether any of those particles had been carried by tire treads from Mexico into the El Paso area or by soles of feet. We have the capability—in this case we used helicopters—to remotely sense the amount of radiation, the type of radiation and the species of radioactive substance through very sensitive detectors. We use transponders which are basically radios to the helicopter, which allows the helicopter to plot exactly where it is. Then you can match its receipt of information from the ground of the radioactive nature against the geographic locations and then plot graphs like are shown there were isoplaths. Those would indicate hot spots which then you can go with ground instruments to those spots to find those little particles.

In fact, what we have done already in the El Paso area is the area that is north of the Rio Grande River, we have flown with our helicopter for the last 10 days, running in grids like this, and we have so far found no trace of a radioactive material on our side. We know that there is material on the Mexican side of the border and we have an oral request which is being put into writing from the Mexican Government—we volunteered our service immediately upon becoming aware of this—to do a survey for them so that they can collect such particles as we find in order to restore the ground to the normal background radiation.

Mrs. SCHNEIDER. I would like to ask you a question on that last point. When was it discovered that you were able to make this determination? How long ago was it that you were in a position where you could identify where these particles had been distributed?

Mr. MARES. The capability has been in existence for many years.

Mrs. SCHNEIDER. I see. In this particular incident dealing with Mexico, when did you recognize that there was a problem within the country of Mexico?

Mr. MARES. It was in January, as I recollect the sequence. I think on the 14th or 16th of January we learned about this when a truck left the Los Alamos National Laboratory and the radiation monitor picked up radioactivity. We tracked down the truck, found out what it was carrying—we collectively, Governmental officials, not DOE but collectively, the State and Federal public health authorities—tracked down the source of that reinforcement rod which was about 3 or 4 days later. So, we have known that the source was basically in Mexico since late January.

Mrs. SCHNEIDER. OK. So, you have the capability of identifying where these particles are?

Mr. MARES. Correct.

Mrs. SCHNEIDER. Now, you didn't say anything about your capability of cleaning it up.

Mr. MARES. We provide the information to identify where the health—to the extent there were particles on our side which we have not found—my understanding here is that we would provide the information down to where the particles are. I am sure, from a technical standpoint, we would provide information regarding how to remove the particles and restore the surface.

Mrs. SCHNEIDER. What is the half-life of the particles that we are talking about.

Mr. MARES. I think they are about 4 to 5 years, if I am not mistaken.

Mrs. SCHNEIDER. Essentially what you are saying is that you can identify where these particles are and you haven't really found any significant number in our country.

Mr. MARES. We have found none in the United States.

Mrs. SCHNEIDER. None in the United States. However, it is only now that we are communicating almost a month and a half later with Mexico.

Mr. MARES. Quite to the contrary.

Mrs. SCHNEIDER. I thought you said that it is only now that you are writing a letter——

Mr. MARES. No, the Mexican Government is finally writing us a letter requesting us to perform this service. We offered this service as soon as we were aware that it was in that area, we were offering through the State Department this capability.

Mrs. SCHNEIDER. But I am curious to know if we have this capability and this accident did occur and the half-life is 4 to 5 years, then what is the impact on the human health of those individuals that may have encountered those particles during this time period. What responsibility are we taking for that?

Mr. MARES. Your concern is well placed. We have tried as best we can and as promptly as we could to make this service available. We do not have the authority to enter another country without their permission. Until they ask us, we can't go. There are some processes within other governments that sometimes take awhile.

Mrs. SCHNEIDER. Did you explain the health impact of the particles that had been dispensed there? Did they realize that this is a critical or catastrophic occurrence?

Mr. MARES. My understanding from the articles that I am familiar with, as well as from listening to my own people, is that the public health authorities in the affected community are aware of the potential hazard, are aware that some people have received very substantial doses. Again, we as the Government of the United States cannot enter another country for something of this nature without their requesting us to do so.

Mrs. SCHNEIDER. Thank you, Mr. Chairman.

Mr. MARES. That is an indication of one of the capabilities for which we are seeking increased funding in this area. Another activity that we have which we are really quite proud of was where this capability and a related capability of the Department was used in testing the Federal Radiological Monitoring and Assessment plan in an interagency exercise at the St. Lucie Power Plant last

week in Florida. This was the first time the emergency response program—we have some pictures here to show you at least where the plant and a map showing several of the key operating centers were down there. This involved many agencies of the Federal Government, FEMA, EPA, NOAA, Department of Energy. The Department of Energy had over 100 people there of its own employees and contractors.

We were basically working through what would happen in the very unlikely event of a nuclear accident and integrating the activities of all of the appropriate governmental as well as local authorities. I think that was a very successful exercise and I think there were things there that we learned that will allow us to be of better assistance in the event that we are called upon in the future for such an activity.

Mrs. SCHNEIDER. Did you have any involvement in Three Mile Island?

Mr. MARES. Our office provided monitoring capability of this type. We have fixed-wing aircraft as well as helicopters that were there within the first 6 or 12 hours to monitor radiation in the air, a capability which we have. We did that as well as ground monitoring under the general direction of the NRC. They are the cognizant Federal authority in the event of a civilian nuclear powerplant accident. Yes, ma'am, we were there.

Mrs. SCHNEIDER. Mr. Mares, I regret that I have a very hectic schedule today, so I have to run out. However, I will say that based on the testimony which I had an opportunity to look at in advance and the oral testimony that you have given me now, I really cannot justify at all the 41-percent increase in the budget. If there are some other line items or specifics that you can supply us, not just saying that you have this or that capability, but that the capability has been utilized or what its end function will be, I might be otherwise persuaded. I will say, given our budget constraints and given the kind of reductions that are being called for in other portions of the budget, this kind of increase, if it has ever been brought up before any committee for any agency, the usual response from the agency is that we could not even absorb a 41-percent increase and be capable of spending it all in a period of time nor would we have the staff available to spend that kind of money.

So, I just wanted you to know where I was coming from because I do have to leave and won't have the opportunity to ask further questions.

Mr. MARES. I would be happy to provide to you or your staff at any time a substantially more detailed breakdown of how every bit of that is spent. I can assure you that in reviewing the requests that we made of our own management and were reviewed by the Office of Management and Budget, there were exceedingly critical reviews made of that request, and in the context of the Department's overall request, which is in no way increased like that, the judgment was made that this is an area wherein the performance and contribution to the overall safe operating mission of the Department warranted a request of this magnitude.

It is made of individual little pieces of projects that are important. I will, as I say, give you the list of each one of them. I don't

think it was an unreasonable increase, and I am convinced it can be well managed.

[The material referred to follows:]

The requested increase in nuclear safety activities is shown in the following table, and the significant changes are discussed below:

Category	FY 1984 Appropriation ($000)	FY 1985 Request ($000)	Increase $'s in Thousands
Emergency Preparedness	$ 6,190	$ 7,700	$ +1,510
Health Physics	1,980	3,200	+1,220
Criticality Safety	590	1,530	+ 940
Training	835	1,340	+ 505
Reactor Safety	875	1,000	+ 125
Process Facility Safety	478	530	+ 52
Nuclear Safety Technology	552	900	+ 348
Total	$11,500	$16,200	$+4,700

The largest increase is the $1,510,000 for emergency preparedness, which will go to expand the operational capability of the unique resources maintained by the Department to monitor and assess any accidental release of radioactivity from a nuclear operation. The increase will be directed largely to the comprehensive integrated remote sensing effort, which will provide extensive multispectral scanning, large format aerial photography and airborne nuclear radiometric information to characterize all DOE sites and to serve as baseline data for comparison in the event of an emergency.

The protection of the radiation worker is directly keyed to our ability to accurately measure his radiation exposure and environment. At the present time, some serious problems in the measurement technology continue to exist. Further, a scientific data base is necessary Department-wide to assist in countering the impracticability of recently proposed national/international standards and regulations. The experience of DOE at the laboratory level must be brought to bear to bring about more realistic standards and regulations. Finally, performance standardization in dosimetry instrumentation is essential to an upgraded DOE radiation protection program. The $1,220,000 increase in health physics will permit greater efforts in these critical areas.

The $940,000 increase in criticality safety is needed to establish a nuclear criticality safety program which has Department-wide applicability. Specifically, the funds would be used to update nuclear safety guides and documents, some of which are over 20 years old, to develop and maintain state-of-the-art computer computational techniques, and to validate an improved measurements capability. We believe these efforts have the potential for permitting significant reductions in safety conservatisms, without compromising the level of protection provided, as more reliable criticality safety information is developed and validated.

Initial efforts in the training program area after the Three Mile Island accident were directed at improvements in policies, requirements and guidelines for selection and training of reactor operations personnel. These efforts are to be continued with emphasis on improving the quality of reactor operator training programs. The $505,000 increase will be used to expand our efforts directed to the training of operating personnel for nonreactor nuclear processing facilities, which is equally important as those for reactor operations. Initiatives in this area will include the application of performance based training methods to chemical process operator training programs, development of generic training materials, and workshops for contractor training managers.

Mrs. SCHNEIDER. Thank you.

Mr. SCHEUER. Mr. MacKay?

Mr. MACKAY. Mr. Mares, I am having to ask some fairly basic questions. This is my first year, and I don't come armed with any divinely inspired inherent knowledge of what you do, and I have to say that your title is sufficiently generic that I don't have any idea of what your responsibilities are. You are the Assistant Secretary for Policy. Does that mean the policy of the Department of Energy?

Mr. MARES. I can understand your question, because it is the first time I have appeared before this particular committee on the particular subject myself. My responsibilities are for the Office of Policy, Planning, and Analysis within the Department which is the office that provides the Secretary and the Department with both review of work that is done of a policy nature on energy matters by other offices of the Department as well as carry the lead on several matters at the Secretary's direction.

The other office for which I am responsible is the Office of Environment, Safety, and Health which is the subject of today's budget request. That office is basically charged with the responsibility to develop the guidelines, internal regulations, for the Department to ensure that the Department's facilities, of which we have about 140,000 people working at our facilities, that they are operated in a safe, healthy, and environmentally sound fashion.

Mr. MACKAY. That is one of the questions I had. Your primary responsibility within safety and environment and health is for the safety and environmental impact of your own programs, not for those of the industry.

Mr. MARES. That is correct.

Mr. MACKAY. This industry, I would assume, are primarily regulated by the——

Mr. MARES. NRC, OSHA, other agencies.

Mr. MACKAY. So, the 40-percent increase in your environment, safety, and health budget is because of a 40-percent enhanced concern on your part for the safety of what you are doing or are going to start doing. Is that it? Within your own Department? Not because you need 40 percent more to regulate or work with other private or public sector agencies.

Mr. MARES. That is correct, but the 40 percent is only with respect to one activity within our office. The total increase is less than a sixth, which would be about 15 percent.

Mr. MACKAY. You have responsibility for manufacturing nuclear weapons.

Mr. MARES. The Department does, yes, sir.

Mr. MACKAY. And this safety program has to do with that?

Mr. MARES. Yes, sir, from an overview standpoint. The line organization which starts with the contractor—I am not sure if Pinellis is in your district or not, but there is a DOE contractor making parts for the weapons program in Florida. The contractor is charged with the responsibility of operating that facility in a safe and environmentally sound manner.

The first line of departmental review is through what we call the operations offices, of which there are eight around the country, each assigned to various facilities or various facilities assigned to them. The budgets for those offices, as it relates to the program,

are presented here by assistant secretaries or directors such as Dr. Trivelpiece here earlier or other assistant secretaries. They have the next line of line responsibility that their operations are done in a safe fashion. Then it goes directly from them to the Secretary.

Separately, our office is charged with providing oversight that we are as an organization paying attention to safety, that we have in place appropriate standards, guidance, regulations, internal regulations, and that we do, in effect, provide technical assistance to these offices. One of the things, for instance, in this increase is to spend some money to increase our instrumentation so we can measure what the effect on humans is of low-level radiation. That is a deficiency in our technical capability and we want to remedy that.

Another area of deficiency is in what is called criticality safety wherein if you get too much radioactive or potentially fissile material close together, you can have a nonexplosive accident. You can have a criticality incident, as they call it.

There has, in our judgment, been a lot of potential knowledge or tools that are available to study this to enhance our knowledge base and it is appropriate for us to seek funds to do that. We are basically an internal regulatory arm as well as an internal technical assistance arm to the organization

Mr. MACKAY. In this subcommittee's oversight function, the 40 percent is a red flag. It says either that you have concluded that you had not had adequate procedures in the past or that you are starting into some new program that has a substantial dimension to it that you did not have before. I am trying to find out is it either of those or is the third which is that you want to plush up the system?

Mr. MARES. Well, it is not the third.

Mr. MACKAY. I knew that. I just thought I would try to give you—if you said neither of the above, I was going to arrive at a worst conclusion.

Mr. MARES. There are some initiatives that we want to start that in a few cases we sought them last year and got less funds than we requested last year, and we didn't agree with that judgment. We are trying again to persuade the Congress that the funds that we are seeking in this program, which are only a small part of the total amount of money that is spent annually on safety matters in the Department through these programs, really you are spending several hundreds of millions of dollars on safety and environmentally related activities.

Mr. MACKAY. Let me get to the underlying question I am trying to raise. Have increased requirements in the DOD budget now begun to show up in your budget and should they be properly categorized as increased costs of the Defense Department?

Mr. MARES. No, sir. I would not interpret the reasons for the increased request to be read into the Department of Defense. There is increased Defense programs activity within the Department of Energy over the last couple of years. That budget has increased by about something over a third in the past 3 years, but our activities are more of an oversight nature and a technical assistance nature, and I think there are some things which we think are appropriate and desirable for us to enhance our abilities in these areas.

We have had, as those statistics show you, as well as other statistics that I have looked at, a really outstanding safety record by comparison to almost anything.

Mr. MACKAY. Yes, I would agree with you.

Mr. MARES. But you can't rest on your laurels. Safety is something that you don't want to go to sleep on. You need to be pushing the technical limits to get better techniques, better instrumentation. We are trying to learn from what industry learned from TMI. We, as a Department, put several $100 million into the facility, upgrading our facilities. We are basically out trying to learn to do a better job, and we think that by doing it our safety record will at least stay where it is and our desire would be to enhance it.

Mr. MACKAY. Does your office have any shared responsibility to do with NRC? For instance, do they inspect any of your facilities?

Mr. MARES. No. NRC does not inspect our facilities. We, as an outgrowth of the Atomic Energy Act and when NRC was set up, retained from a nuclear safety standpoint responsibility to set the guidance and inspect and regulate, if you will, our nuclear facilities.

Mr. MACKAY. Do your facilities comply with——

Mr. MARES. I take it back; I have made it too absolute. There are a couple which were subject to NRC regulation. I think the nuclear waste repository program and, if I am not mistaken, the Clinch River breeder was, and there may be a third. However, by and large, the Defense and test reactors that we have are regulated by our Department.

Mr. MACKAY. The whole question of dismantling facilities at the end of their useful life and how those costs will be incurred, are you already into that and do you coordinate that with NRC? In other words, are they learning from your experience and are you learning from theirs?

Mr. MARES. To the best of my knowledge we are, and it is something that I would certainly—each of us is trying to learn from the other.

Mr. MACKAY. Who has that responsibility within DOE? Would that be you?

Mr. MARES. On relations with NRC or on the termination of facilities?

Mr. MACKAY. Both.

Mr. MARES. In terms of relations with NRC, there is a memorandum of understanding between the agencies and a coordinating committee that meets, I think, quarterly, staff of both agencies and then at the senior management level it meets at least once annually, involving Mr. Dirks and other of the senior members on the annual meeting. The other ones are of the division heads and office directors and they meet more frequently.

In terms of the ultimate decommissioning and decontamination of facilities, the Department has underway at Shippingport that process for that reactor. I can't remember whether that is being done by the Office of Nuclear Energy or the Office of Naval Reactors. It is not our office, but the line responsibility and the funding for it is, I think, in the Office of Nuclear Energy.

Our role would be to establish guidance from an operational safety and a nuclear safety standpoint. Our role would not be to be

the program responsible for it, which actually answers another question that someone brought up.

In one of our programs we are seeking less money than last year. Part of the reason is that we did transfer some operational activities to a different office. Therefore, we requested less money.

Mr. SCHEUER. Therefore you requested what?

Mr. MARES. Therefore we requested less funds in 1985 than we had in 1984 because an activity was transferred to a different office within the Department which has requested funds for that, and that was in one of the remedial action programs.

Mr. MACKAY. In the joint exercise with the FP&L plant, I don't exactly understand what the goal of that was and what was accomplished by that. I think it was an excellent idea. I think it would be great to have a dry run like a drill on these facilities, and I am hoping that is being done, but from what you have said, I would have expected NRC to be doing that and not you.

Mr. MARES. This was all Federal agencies that have involvement. If I understand correctly, every nuclear power plant has to do at least one test of its emergency plan each year. This test that was done last week was done in conjunction with the annual test being done by the Florida Power & Light Company at St. Lucie. It was a first time that the Federal Government has marshaled physically in the field its resources as if there had been a nuclear incident since Three Mile Island. There were NRC people there, and in fact NRC is the cognizant Federal authority because they are the group that regulates this particular reactor. NRC was present along with EPA, NOAA, Department of Agriculture, ourselves, FEMA, and several others as well. The State government was involved and there were two counties involved.

Mr. MACKAY. Was it your impression that the thing would have worked?

Mr. MARES. Yes.

Mr. MACKAY. With all those people there?

Mr. MARES. Yes. From my observations, I think they did very well.

Mr. MACKAY. Do you do that at your facilities?

Mr. MARES. We have plans and we periodically test them. We have not done a test of the type that was done at St. Lucie.

Mr. MACKAY. Do you think it would be worthwhile?

Mr. MARES. The Department of Energy had representatives at St. Lucie from each of the eight Operations Offices. Those offices, in turn, have responsibility for their facilities within their areas, so I think the Department learned a lot by participating in this exercise and that will feed back into our own emergency planning activities.

Mr. MACKAY. It would seem to me that in the area of emergency planning there could be a good case made, if not in other areas, that your procedures should be identical with NRC's, because both of your agencies are trying to interface with State and local governments who have to understand what the plans are. From my knowledge of State and local government, you are asking a great deal to get them to understand one plan, much less two. Have you given any thought to having a single emergency procedure? In other words, is there a reason not to have?

Mr. MARES. My understanding is your observation has been made internally and is a very rational observation. For instance, at Richland, WA, where the Hanford works are, there are also nuclear powerplants. My understanding is that the emergency plans for the Department of Energy as well as the commercial plants are identical. I don't have information on the other locations, but I have been very impressed with the rationality of the people as we have looked at these things and would expect an attempt to try to have it be as compatible as possible.

Mr. MACKAY. Thank you, Mr. Mares.

Thank you, Mr. Chairman.

Mr. SCHEUER. I just want to address a question or two to you on the subject of acid rain. On page 11 of your statement, you indicate that your office will continue to participate in departmental assessments concerning acid rain and other transboundary air pollutants. What is the role of your office in determining acid rain control policy for the Government and what activities are underway regarding acid rain and other transboundary pollutants?

Mr. MARES. Within the Office of Environment, Safety, and Health, we have an office that is known as the Office of Environmental Assessment. That Office performs analysis of environmental proposals, be they regulations, laws, or whatever, based upon the skills that are available to us and the experience available to us from the national labs and elsewhere on matters like acid rain. In addition, within the Office of Policy, for which I am also the Assistant Secretary, there is an environmental policy group that is also looks at acid rain from a policy standpoint. So, the Department's policy positions and analytical resources concerning environmental issues reside in large measure within the Office for which I am the Assistant Secretary and that would include transboundary air pollutants.

From a scientific standpoint, the investigation of transportation of pollutants across boundaries and distances, the research in that regard is being done under the auspices of the interagency acid rain task force. There is work on modeling, computer modeling of that transportation.

Our Department, primarily through the Office of Energy Research under Dr. Trivelpiece, is funding about $5 to $6 million for that activity in fiscal year 1985.

In short, my Office works on policy matters. Dr. Trivelpiece's, as well as the Office of Fossil Energy, do the scientific research and development work out of which the information is then available to everybody for reaching their own conclusions about what is appropriate strategy.

Mr. SCHEUER. You took a little unbrage with my characterization of your policy on acid rain when I suggested that the policy is that we have to know everything before we can do anything. If that is not the policy of this administration, maybe you could explain to me what it is. What is the policy of this administration?

Mr. MARES. I will try in about two sentences to suggest that the uncertainties that exist before we believe one should embark upon a regulatory program are such that the acquisition of additional knowledge to reduce that level of uncertainty is a wise course of

action. If you would like I could take a few more—I don't know how much time you have got——

Mr. SCHEUER. I have time. This is a very important question to us. We seem to feel that the evidence is rolling up that widespread damage is taking place. The folks out at Boulder, CO, were saying for years, Bill Hess was saying for years, that we really didn't know enough to legislate significant regulatory programs. He is not saying that anymore, and many other very careful, thoughtful, conservative scientists who were saying for several years, while we were dancing up and down in outrage up here waiting for you to do something, they were justifying your inaction.

They are now saying yes, we surely know enough to do something. We may not know enough to do everything and we may not know enough to engage in multibillion dollar programs, but surely we know enough about the devastation that is taking place along the eastern seaboard of Canada and the United States and going out west to really the west coast, we know enough about the devastation that has taken place in the Adirondacks area that band aids are not enough and that there is more that we can do that is sensible, that is cost effective. That is our position.

You folks seem to be standing or sitting over there figuring out how many angels can dance on the head of a pin while the devastation goes on.

If your policy isn't to defer any action until we have total knowledge, what is it?

Mr. MARES. The policy recognizes there are quite a few uncertainties, not the least of which is that the amount and extent and trend of the damage in the forests as well as the lakes is not well defined.

Mr. SCHEUER. The trend is not well defined?

Mr. MARES. That is correct. The trend in the damage is not well defined, sir, to the best of my knowledge based on the readings that I have done as well as talking to the people on our own staff, as well as talking to the people on EPA's staff. Furthermore, what we are talking about is whether additional emissions control beyond what is already covered in the Clean Air Act is warranted. The Clean Air Act does cover all of the precursors to acid rain.

Mr. SCHEUER. I am not limiting myself to emissions control. I am talking about the whole spectrum of possible remedies.

Mr. MARES. This is one of the points that I made in the testimony yesterday, that quite a few proposals have been made intermediate between continuation of the Clean Air Act with no change although even it admits of change in terms of changing restrictions as technology is enhanced, all the way through to the rollback proposals, of which there are a large number. So, there is a variety of approaches that have been presented that could and should appropriately be considered.

In order to intelligently consider those as against the uncertainties is what we are trying to get information and plan to have information of increasing level of understanding over the ensuing years.

Now, let me try to finish what the other uncertainties are because I think they are relevant and to be considered. You have to think, among other things, what actually would one seek to con-

trol? Would you seek to control the sulfur oxides, the nitrogen oxides, the volatile organic compounds? Particulates or oxidants? Do you seek to—when do you seek to control? If you accept that the trends in damage may be slow, measured in decades and not in months or years, there are substantial powerplants that are going to be retired at periods of time over the ensuing years. The replacements thereof have to meet—these were the plants that were built before the Clean Air Act came into effect—so the emissions on the replacement plants have to be substantially less than those of the plants that are currently in place.

Mr. SCHEUER. Do you think we ought to have legislation mandating retirement of these plants at a certain period of time after a certain number of years of use?

Mr. MARES. There is, in fact, a proposal along that line that I believe Congressmen Broyhill and Madigan have made basically suggesting that that would be an approach that ought to be considered.

Mr. SCHEUER. What do you think?

Mr. MARES. I think it is one that needs to be analyzed to determine whether it does make sense.

Mr. SCHEUER. Well, what is holding you back?

Mr. MARES. We are doing those studies.

Mr. SCHEUER. When will you have some answers for us, some judgments?

Mr. MARES. I would rather not speculate as to when those studies are going to be finished and for sure I am not going to speculate what the outcome or judgment is going to be on that. It is not simply a one person judgment. It ultimately ends up being an administration judgment on those matters. But I would confirm to you that those are the sorts of things that at least our office, including the funding that I am requesting here, will be applied to try to enhance the understanding of what are the significance of courses of action other than the rollback one or the——

Mr. SCHEUER. What are some of the other approaches that you are looking at with interest?

Mr. MARES. I am making no judgment as to whether we are supporting or prospectively would support or not. I am simply suggesting to you that these are ideas that have been presented by thoughtful people and warrant evaluation.

Mr. SCHEUER. I am asking you, what are some of these ideas that you are looking at?

Mr. MARES. They include amending the Clean Air Act in a way that would give greater administrative flexibility to EPA to decide when and how to use some enhanced authorities related to emissions control. Another is——

Mr. SCHEUER. In other words, you would give them some kind of standby authority?

Mr. MARES. The merit of that idea or an idea along that line has been proposed and it is one that ought to be reflected upon.

Mr. SCHEUER. Right. What other ideas are you thinking about?

Mr. MARES. Whether one tries to target the control strategy to the most sensitive receptors, meaning do you target it toward urban materials, visibility in the West, sensitive aquatic areas? And can you target to, in effect, the particular receptor areas that

are most sensitive rather than more broadcast, more general types of approaches. And there are variations within those. I have elaborated a bit in the testimony which I referred to in my very opening remarks. I have got a copy which I will give you for the record.

Mr. SCHEUER. Excellent.

Perhaps some direct approach to the problems of the Adirondack area rather than to try to blanket the United States with a single uniform policy it would be directed toward specific sensitive areas.

Mr. MARES. Along that vein, part of the administration's proposal was to provide funds that would be used by the Department of the Interior in connection with the States to embark upon liming programs to mitigate damage within identified lakes as of today. That program or one similar to that is underway in Sweden in which, if my understanding is correct, they lime about 1,000 lakes a year, or have about 1,000 lakes that they have under that program.

Mr. SCHEUER. I think they are mad as Hell that they have to do that and they have been unable to exert any influence or pressure on the British, the French, the Germans, the Dutch, the Belgians to moderate the pollutants that they are generating in the industrial belt of Europe that float right up to Sweden with the prevailing winds the same way perhaps three-quarters of the pollutants that affect Canada come from our side of the border. Believe me, this is not their desired choice. I have spoken to Swedish scientists and government officials. They would a hell of a lot rather get to the pollution at its sources, but they can't get at these other countries. They have the problems of pollutants that cross transnational boundaries.

We don't have that. Most of our pollutants originate within the continental United States. There are some that come down from Canada, but that is not the main problem. They cross borders, but they are mostly State borders. We do have the luxury of being able to think of comprehensive, holistic answers to this awful problem that the Swedes do not have the luxury of considering because they have other sovereign powers that they have to consider who are dumping their laundry on Sweden. They are dumping their filthy laundry on Sweden and Sweden has no option but to lime lakes.

When you suggest that liming lakes is a grand idea and a very happy solution, I have to tell you that I don't think the Swedes would agree with you that that is anything but a pitifully inadequate paliative in the absence of measures to really get at the problem that is generating their problem. The problem is the industrial belt of Europe that is generating all those pollutants that end up in Sweden, just as the Ohio River Valley generates those pollutants that pollute the east coast of the United States and eastern Canada.

Mr. MARES. With all due respect, I don't think that there is a total agreement that the distant sources are the only source of potential impact on it, whether it is the Adirondacks or any other particular source in our country.

Mr. SCHEUER. Nobody says they are the only source. This subject is so complicated and there is so much that we don't know about transport which is so incredibly complicated that when the scientists start explaining it to me, my eyes glaze over. There is an

awful lot that we don't know and there are very few absolutes that you could make, but it seems to me that one absolute that you can make is that you don't have to know everything before we do anything.

What I am asking you is, when do you think you will have the knowledge base to do something? I think that is what the Congress wants to know, both Houses of the Congress, both parties in both Houses. There is quite a remarkable degree of unanimity here between the House and the Senate, Republicans and Democrats. I have not noticed leading Members of the Senate who happen to be of the Republican faith standing up and defending the Administration's posture on this matter. There is a great deal of unhappiness with the Administration's posture, and what I am trying to do is to help you show us a light at the end of the tunnel. When do you think you will have a sufficient knowledge base to let us know that there are a few things that we can do, perhaps not everything, perhaps not the ultimate, but some paliative measures? Can you give us a timeframe?

Mr. MARES. I think that the answer is measured in a few years, not in a few months and not in a few decades.

Mr. SCHEUER. How much is a few years?

Mr. MARES. Well, I think there is underway——

Mr. SCHEUER. Just tell me what a few years would be.

Mr. MARES. I would say 3 to 5.

Mr. SCHEUER. Pardon?

Mr. MARES. I am saying 3 to 5.

Mr. SCHEUER. Three to five. Starting from the beginning when we really started our acid rain research?

Mr. MARES. When we started it, as I recollect, it was a 10-year program, if I am not mistaken.

Mr. SCHEUER. Yes.

Mr. MARES. We are beginning to reap some of the benefits of that program. There is an assessment of effects that is going to be issued within the next fiscal year. It is one of the things that money is being requested for. There will be increasingly elaborated upon effects assessments given in 2-year intervals in 1987 and 1989.

With the increased activity in terms of both extent of monitoring of effects that is underway now, to the extent that that would indicate the trends in damages or extent of damage is significantly different from what we have seen to date in terms of trends, that could mean or probably would mean that some form of control action should be more seriously considered sooner rather than later.

Mr. SCHEUER. Of course. That is our whole point.

Mr. MARES. I understand that.

Mr. SCHEUER. If you want to engage in a drastic scrubbing program which costs billions of dollars, as the Japanese have already done, based on the data that is available now. It has apparently been satisfactory to them. Let's say that the ideal program that will cost many billions or tens of billions of dollars, perhaps maybe that wouldn't be justified now. Isn't there some paliative program that you could justify now by the present state of our research? Isn't there something we can promise our Canadian friends that we will do? You know, they are very bitter. They are very bitter and

unhappy. They are very outraged. They are very offended by our policy. Can't you hold out a little light at the end of the tunnel and say well, look, we are not going to defer any program indefinitely. At least, we think we can justify this kind of a basic minimum program now.

As our research matures and as it gets more definitive, we will be doing more, but at least right now we think this level of remedy is cost effective and sensible. Can you hold out any hope to our Canadian friends?

Mr. MARES. Let me elaborate on why the problem is complicated and why I don't want to pick a particular year to, for the sake of argument to use your words, to hold out hope for the Canadians. When you project the amount of emissions of sulfur oxides and nitrogen oxides out into the future, you have available to you a series of assumptions that you can make dealing with what the economic growth of the country is going to be, what the retirement of the power plants is going to be, what the use of nuclear power is going to be, all of which are going have enormous influence on how much the emissions of sulfur oxides and nitrogen oxides are going to be.

Depending upon your set of assumptions around those three factors primarily but others as well, you can project that the amount of emissions over the next 20 years of sulfur oxides in the broad northeastern part of the United States from the Mississippi eastward and above the Tennessee line, that the emissions would either be slightly higher for 10 to 15 years and then dropping flat for that period and then drop a bit—in a few cases, they drop a bit maybe in 10 years and then they drop more sharply.

The long-term trend of expectations on emissions is that the sulfur oxides particularly from the powerplants, will drop. You weigh that against the judgment which some people disagree with, but it is our judgment that the trends in effects and damages are very slow and they may not be in effect getting worse, they may be neutral, you are hard pressed to——

Mr. SCHEUER. I don't understand that. They are cumulative, aren't they? What does neutral mean in that context?

Mr. MARES. It depends. Again, here is where we are up against local effects. Certainly the effect on materials within an urban area could be cumulative, yet we have the ability——

Mr. SCHEUER. Cumulative.

Mr. MARES. Yes, I say could be cumulative. If you look at statuary or you look at others——

Mr. SCHEUER. Could be. They are cumulative, aren't they? Are they cumulative?

Mr. MARES. I would think that is right. But the point is that we do have controls, systems in place to address impact on the local materials. The local sources there, I think everybody would acknowledge, are much more significant than they are in terms of the rural forests, parks, lakes, rural areas of the country. Relative to the lakes issue, I am not sure that there is a unanimity or even a strong consensus on the cumulative effect, in effect, arguing that it is not reversible. The materials damage in the cities, I have never heard anybody say that that is reversible.

Mr. SCHEUER. I didn't say these effects are irreversible. What I am suggesting is that they are cumulative, and there is nothing

benign or neutral about the process that goes on, even though it is a slow process; it is inexorable and it is cumulative. It is an incremental add-on every year to the total damage as of the year before and the year before that.

Obviously, at some point in time, if you remedy the situation and you drastically cut down on emissions, we would hope to reverse that process.

Mr. MARES. Well, let me point out something historical that I don't think people realize.

Mr. SCHEUER. Well, we have to be out of this room by 4 which gives us only a couple of minutes.

Mr. MARES. The total emissions of sulfur oxide in this country have dropped over the last 10 years. That is not generally publicized, but we have gone from about 31 million tons, as I recollect, to about 27 million tons. We peaked in about 1970, if I am not mistaken. Therefore, one could argue that, because of that, we are in better shape than we were before and that there may be a lagtime in terms of what we are seeing.

The argument about cumulative that you are making, I don't profess to be a scientist in this area. I have listened to a lot of the scientists in this area. I have not heard that argument.

Mr. SCHEUER. Let me make it perfectly clear. I am not a scientist. Whatever I know, I have gleaned from scientists, but I am hardly a scientific authority.

Why don't you just take 1 or 2 more minutes and wind up your testimony on this point. If you can hold out some hope for the Canadians, that would be wonderful. If you can hold out a glimmer of hope for the Congress, both Houses, both parties, that would be wonderful. If you can't, we will try to cope with that.

Mr. MARES. I happen to have hope that the enhancement of knowledge that will occur over the next several years, both in terms of understanding the nature of the problem as well as in terms of the technologies available to us to try to reduce effluents, thinking in terms of the fossil energy control technologies, for instance, will allow us, as a society, to more intelligently fashion any change from our current act in a way such that the benefits to society will exceed the costs. That would be my conclusion.

[The prepared statement of Mr. Mares follows:]

STATEMENT

OF

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POLICY, SAFETY, AND ENVIRONMENT

U.S. DEPARTMENT OF ENERGY

BEFORE THE

COMMITTEE ON SCIENCE AND TECHNOLOGY

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCh AND ENVIRONMENT

U.S. HOUSE OF REPRESENTATIVES

MARCH 13, 1984

Statement of Jan W. Mares
Assistant Secretary for Policy, Safety, and Environment
Department of Energy
House Committee on Science and Technology
Subcommittee on Natural Resources,
Agriculture Research and Environment

Mr. Chairman and members of the Subcommittee, I am pleased to be here today to discuss with you the Department's budget request for FY 1985 for the Office of Environment, Safety and Health. With me to assist in responding to your questions is Robert W. Davies, the Deputy Assistant Secretary for Environment, Safety and Health.

NATIONAL ENERGY POLICY PLAN AND SAFE, ENVIRONMENTALLY SOUND OPERATION OF DOE ACTIVITIES

The overall goal of our national energy policy is to foster an adequate supply of energy at reasonable costs. The two strategies to achieve this goal are (1) to promote a balanced and mixed energy resource system and (2) to minimize federal control and involvement in energy markets while maintaining public health and safety and environmental quality. The Department of Energy implements these strategies through many programs involving diverse activities from research and development like magnetic fusion to process services like uranium enrichment. In addition, the Department is responsible for the manufacturing of nuclear weapons for national defense purposes. The DOE Organization Act establishes the Departmental goal of protecting and enhancing environmental quality and assuring public health and safety.

Differently stated, the Department's goal is for all of its activities to be operated in a safe, healthy and environmentally sound manner.

The Department's health and safety record has been outstanding by any standard. Its environmental record has also been good and there are no substantiated cases of impact on public health from the Department's operations, even though there have been occasional allegations to the contrary. The Department has always been a leader in environmental protection through its research activities to define and avoid adverse environmental impacts from its operations. The Department has also made continuing efforts to be in compliance with applicable environmental requirements as they have changed through the years. In fact, planning is currently underway to modify certain previously acceptable practices to meet current standards.

The Headquarters Environment, Safety, and Health (ES&H) functions are to establish departmental policy, provide guidance and technical assistance, oversee implementation of policy and guidelines, and perform an independent overview and assessment role for the Secretary. The line organizations starting with the DOE contractor, continuing through the DOE operations office and the program office, have responsibility and accountability for the safe, healthy and environmentally sound performance of their activities.

Thus the ES&H Office has overall responsibility for establishment and oversight of policy implementation by line organizations to assure safety and health of the workers and the public, and protection of the environment at DOE's operations.

GOAL OF OFFICE OF ENVIRONMENT SAFETY AND HEALTH

The goal of the Office of Environment, Safety and Health is to assure safe and environmentally sound operation of DOE activities. This is done by providing the Secretary and the Department a competent, adequate, independent oversight capability at headquarters which (i) as appropriate reviews, assesses, appraises and in some cases approves, Departmental (including contractor) activities; (ii) develops appropriate policies, standards and guidance for DOE; (iii) identifies and supports research to assist DOE to operate in a safe and environmentally sound manner; and (iv) provides related technical (including quality assurance) assistance to Departmental activities to assist them in operating in this manner. These functions are performed while recognizing the unalterable responsibility of the line organizations for safe and environmentally sound operation of the activities under their supervision.

The recent realignment of functional responsibilities within the Department placed the Office of Environment, Safety and Health under the Assistant Secretary for Policy, Safety, and Environment. This change eliminated the previous split

in management focus whereby the Assistant Secretary was responsible for both safety and environmental oversight as well as for several major outlay programs which required substantial management attention. The change will result in increased management attention to the Department's environmental programs and its nuclear and operational safety functions. This in turn is expected to bring about an increased emphasis Department-wide on the safe, and environmentally sound operation of DOE activities.

The Environment, Safety and Health Office provides to the Secretary and other senior managers of the DOE an independent overview assessment of, and technical assistance to the Department's management of its facilities to assure safe and healthful workplace conditions, the safety and health of the public, protection of the environment, and compliance with applicable ES&H-related statutory and regulatory requirements. The office also assures that energy issues compatible with national energy goals are considered in the development of proposed environmental requirements.

Achieving the Department's environmental, safety and health protection and quality assurance objectives hinges on a solid partnership between the Environment, Safety, and Health Office and the Department's line programs. The ES&H Office furnishes the line programs with applicable ES&H requirements through general policy orders, monitors their efforts in complying with

these requirements, and assists with technical advice in resolving implementation problems. This allows the line organizations, which have the principal responsibility for safe and environmentally sound operations, to proceed with greater assurance that they will not incur interruptions from accidents or litigation stemming from non-compliance with ES&H-related laws or practices.

OUTSTANDING SAFETY AND HEALTH RECORD

The Department's safety and health record in 1983 was outstanding. The Department has the safety and health responsibility for 157,000 Federal and contractor employees who operate facilities with a property replacement value of about $65 billion. The Department's fatality, injury, and illness rates for FY 1983 were not only well below the rates of the private sector, (i.e., only 1/5th of the private sector's fatality rates and better than 1/3rd of the private sector's recorded illnesses and injuries rates), but also below the Department's own averages of its annual rates for the period 1978 through 1982. None of the FY 1983 injuries or illnesses were caused by radiation exposure, and there were no accidental exposures in excess of the various allowable annual limits. The total reported property loss for the Department in FY 1983 was approximately $3.1 million. The loss rate was approximately half a cent for every hundred

dollars of property valuation which is a significant improvement over the latest 5-year annual average for DOE of .89 cent per hundred dollar valuation.

The accidents per million miles and dollar loss per 1,000 vehicle miles rates were less than one-half the comparable rates for all nation-wide travel, as reported by the National Safety Council. The Department also owns or contracts for 48 aircraft, none of which were involved in an accident. In addition, there were no marine or railroad losses reported during FY 1983.

Of the 85,000 employees routinely monitored for radiation exposure, only 43% received a measurable dose in 1982, the latest calendar year for which complete information is available. Of these, only 1.6% received a dose greater than 1 rem and no employee received a dose in excess of the allowable 5 rem limit.

The safety and health record indicates that the Department's performance in all areas continues to be far better than comparable rates for the private sector.

PRINCIPAL STATUTORY AUTHORITY

The statutory authority governing the ES&H Program includes the DOE Organization Act which establishes a Departmental goal of

protecting and enhancing environmental quality and assuring public health and safety; the Atomic Energy Act which exempts DOE and its contractors from certain licensing requirements (The DOE requires that the Department's operations be conducted in accordance with comparable health and safety practices.); and the National Environmental Policy Act. This Act requires consideration of environmental factors in agency decisionmaking, including as appropriate, the preparation of environmental assessments and environmental impact statements.

PROGRAM ORGANIZATION

The Program's functions are carried out by five major components: Nuclear Safety, Quality Assurance and Standards, Operational Safety, Environmental Compliance, and Environmental Analysis. Their activities include the development of policies and standards; oversight to monitor program and field office performance in complying with DOE policies and standards, technical and policy guidance assistance to foster compliance; the review of National Environmental Policy Act documents; and the analysis of energy/environmental issues.

FUNDING

In FY 1985 we are requesting $37.1 million for the Environment, Safety and Health Program which is $5.0 million more than

appropriated in FY 1984 as noted in the following table, and discussed in the following sections. The increase is primarily in the nuclear safety area even though the Department's nuclear safety record has been outstanding. The planned increase is considered necessary by the Department to assure the continued safety of operations and to improve on the Department's excellent safety record. It is primarily in health physics for improving and standardizing plant measurement and operating procedures, in emergency response by enhancing the remote sensing capabilities of the Aerial Measurement System, and in criticality safety by upgrading the safety assessments and the safety training for affected contractor and DOE employees. The remaining activities will continue at essentially the same level of effort as in 1984.

Funding Summary

(Budget Authority in Millions)

Environment Safety and Health	FY 1984 Appropriation	FY 1985 Request
Operating Expense:		
Nuclear Safety	$ 11.5	$ 16.2
Quality Assurance and Standards	0.9	1.0
Operational Safety	8.8	9.2
Environmental Compliance	1.5	1.7
Environmental Analysis	2.4	2.6
Program Direction	5.4	4.9
Subtotal	30.5	35.6
Capital Equipment	1.6	1.5
Total ES&H	$ 32.1	$ 37.1
Staffing - Full-time equivalent	95a/	95a/

a/ Excludes 2 FTE's budgeted under the Nuclear Waste Act Fund.

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FY 1984 PROGRAM PLANS

The FY 1984 plans include:

- Conducting comprehensive environmental protection, safety, and health protection appraisals of three field organizations and of two Headquarters program offices. A comprehensive appraisal is comprised of in-depth appraisals of up to 10 functional ES&H areas performed in conjunction with, and as input to, a management appraisal of the organization being appraised.

  This comprehensive appraisal effort has resulted and is expected to continue to result in numerous ES&H improvements such as: enhancing the quality of field office reviews of nuclear facilities and upgrading overall contractor surveillance, through design reviews, construction monitoring, etc.

- Providing training to DOE and DOE contractor personnel in the areas of Human Factors, Nuclear Criticality Safety, Quality Assurance Awareness, and Prevention of Significant Nuclear Events.

- Expanding the criticality safety activities including the upgrading of the statistical measurements technical manual, used throughout DOE operational functions to insure control of fissionable material liquids, to include the latest up-to-date data.

- Testing the Federal Radiological Monitoring and Assessment Plan in an interagency field and headquarters level exercise with NRC, FEMA, state and local authorities and The Florida Power and Light Company personnel at the St. Lucie Nuclear Power Plant on March 6-8, 1984.

- Continuing field testing of prototype improved neutron measurement devices for workplace application.

- Conducting quality assurance surveys of Bonneville and Western Area Power Administrations to determine the status of policy implementation, thereby completing the initial base-line surveys at all major DOE sites, and performing in-depth quality assurance appraisals of four selected major projects (namely the Fuel Materials Examination Facility at Richland, the Assembly Facility at PANTEX, the Uranium Enrichment program at Oak Ridge, and the Crystaline Rock radioactive waste project under Chicago Operations Office) to determine adequacy of their quality assurance programs and activities to meet their needs and objectives.

- Issuing guidance to Headquarters, field, and contractor organizations for the conduct of environmental protection appraisals and audits incorporating industry practices.

- Implementing revised environmental assurance procedures for the DOE Remedial Action Program.

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- Conducting fire protection surveys of five DOE sites (namely Brookhaven Laboratory, Bendix Plant at Kansas City, Mound Laboratory, Sandia in Albuquerque, and Argonne-West in Idaho) and issue initial guidelines for optimum fire management systems for fire environments specific to DOE.

- Completing action on about 600 requests from DOE programs for NEPA-related support, including: about 200 analyses to determine/confirm the level of NEPA documentation required for DOE actions, i.e., Environmental Impact Statement (EIS), Environmental Assessment (EA), or neither; and about 120 independent reviews of EIS's and EA's.

  Major EIS' include those for: the restart of L-Reactor; the Process Facility Modification at Hanford; the Special Isotope Separation Project; the Fuel Processing Restoration Project at Idaho; Bonneville Power Administration's Expanded Regionwide Weatherization Program; the Niagara Falls Storage Site Remedial Action Project; the Salt Lake City Remedial Action Project; and the Manitoba, Dakota, Nebraska (Mandan) 500 KV transmission line from Manitoba thru the Dakotas to Nebraska.

- Continuing to participate in Departmental assessments concerning acid rain and other transboundary air pollutants. Much of this work will be in interagency or international forums.

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FY 1985 OBJECTIVES

In FY 1985 the Program plans to expand the overview and assessment efforts of Departmental activities to assure that environment, safety and health policies are effectively implemented. The principal objectives in FY 1985 include:

- Developing better training guidance for reactor and nuclear facility operators to improve operational safety at DOE nuclear facilities.
- Maintaining and improving the radiological emergency response capability for DOE facilities.
- Developing improved methods for measuring and assessing the amounts of inhaled or ingested radioactive materials to assure compliance with radiation exposure limits recommended by national and international authorities.
- Developing and implementing improved methodologies, particularly in the area of criticality safety, for assessing the safety of nuclear operations.
- Issuing revised environmental protection, safety and health protection guidance and conducting appraisals of ES&H performance at three Operations Offices.
- Issuing improved quality assurance and unusual occurrence reporting guidance based on the analysis of the initial base-

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line survey completed in FY 1984; and appraising implementation of the guidance at six field or program offices.

- Assisting DOE organizational units in preparing sound NEPA documents and performing reviews of all such required documents to facilitate Departmental programs.

- Analyzing proposed regulations and statutes, such as modifications to the Clean Air and Clean Water Acts, to ascertain the potential impact on DOE program or interests.

SUMMARY

The ES&H policies and independent overview have helped the Department to continue its excellent record of safety, health protection, and environmental compliance at the Departmental operational facilities.

The Environment, Safety and Health Program to date has assured that national energy policies and departmental plans, programs and operations have effectively addressed and expeditiously resolved environmental and safety problems. The proposed FY 1985 budget request provides the resources necessary to continue a strong independent Environment, Safety and Health overview of Departmental operations and activities.

I am prepared to answer your questions or comments on this program.

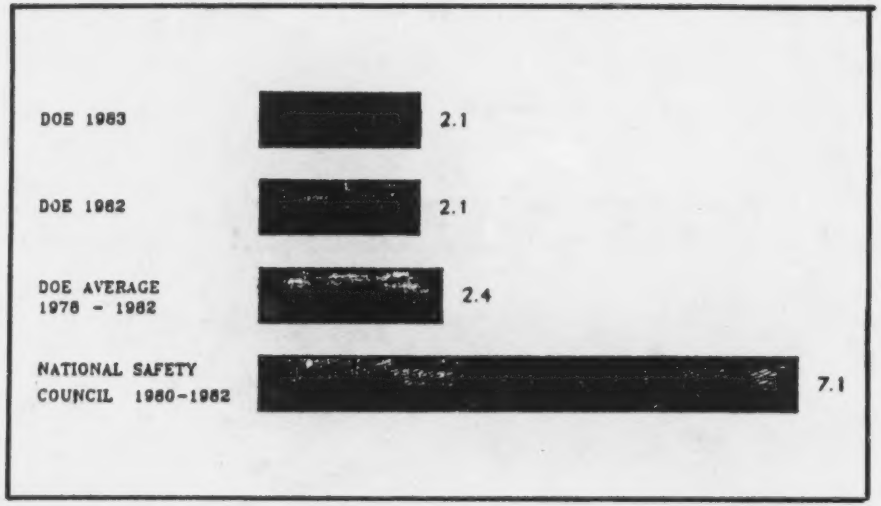


Figure 2. Recordable Injury/Illness Incidence Rate (Cases Per 200,000 Workhours)

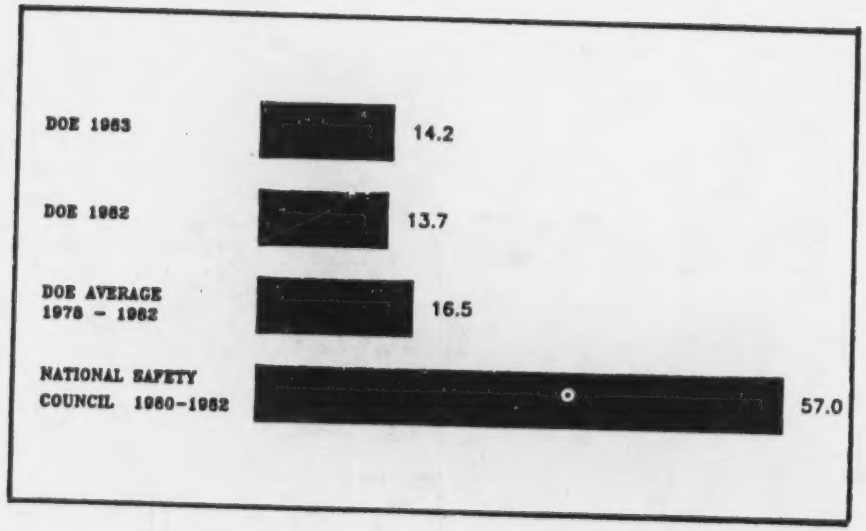
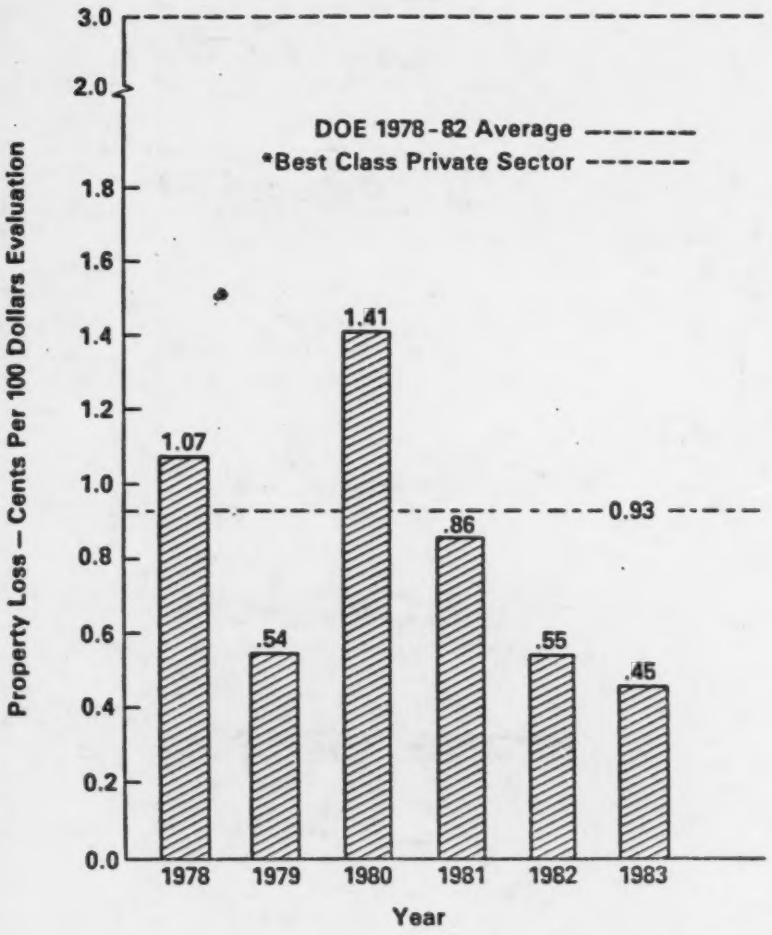
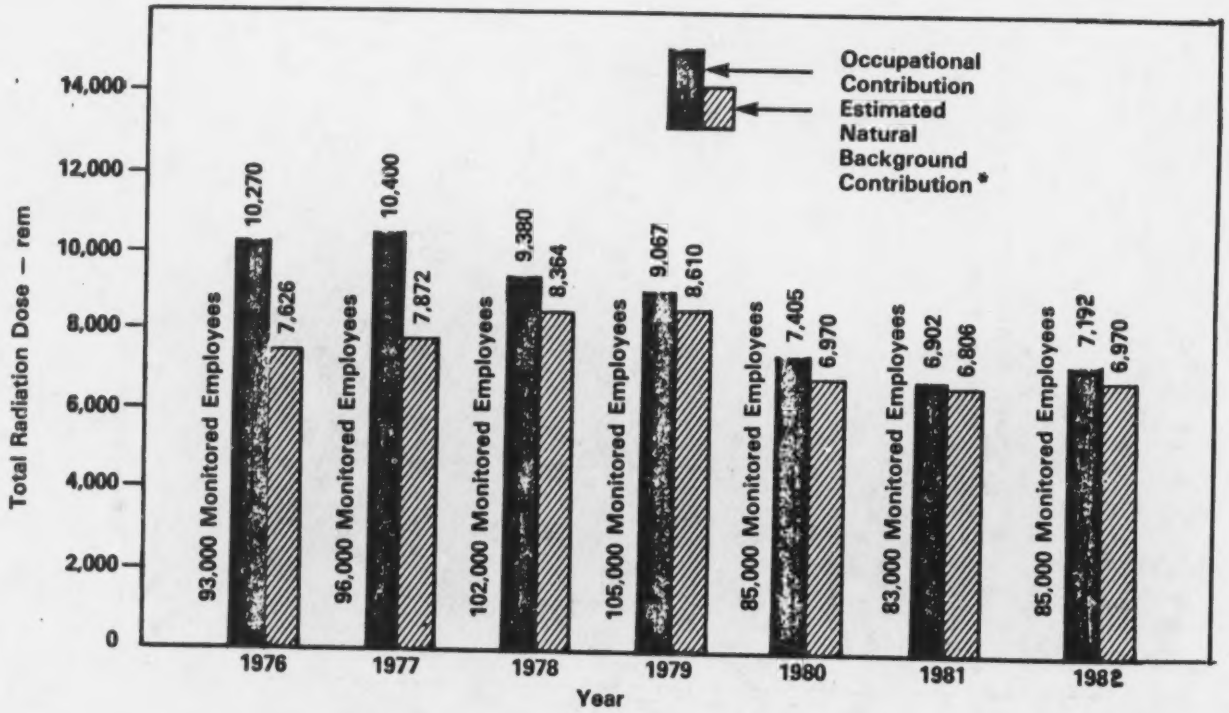


Figure 3. Lost Workday Incidence Rate (Days Per 200,000 Workhours)



*From discussions with engineering personnel from the fire insurance groups.

Figure 3. DOE and Contractor Total Property Loss Rates



* This assumes an average exposure level

Figure 11. Comparison of Total Radiation Dose Received by DOE Monitored Employees and Dose Received from Natural Causes

18

EMPLOYEE EXPOSURE DOSES
GREATER THAN 2.0 REM

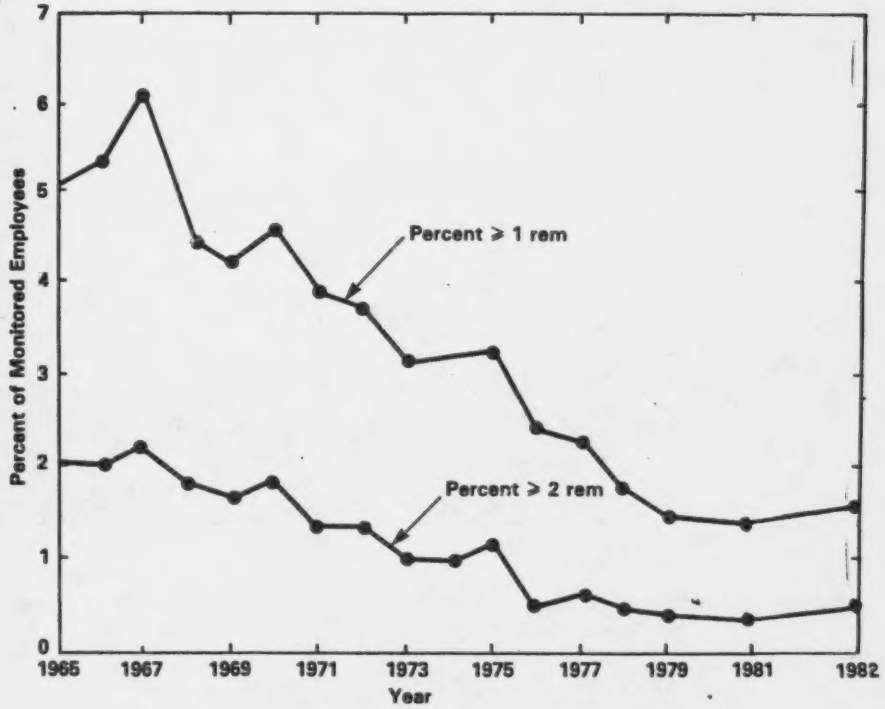


Figure 10. Percentage of Employees Receiving External Doses Greater than 1 Rem and Greater than 2 Rem (5 Rem per Year DOE Standard)

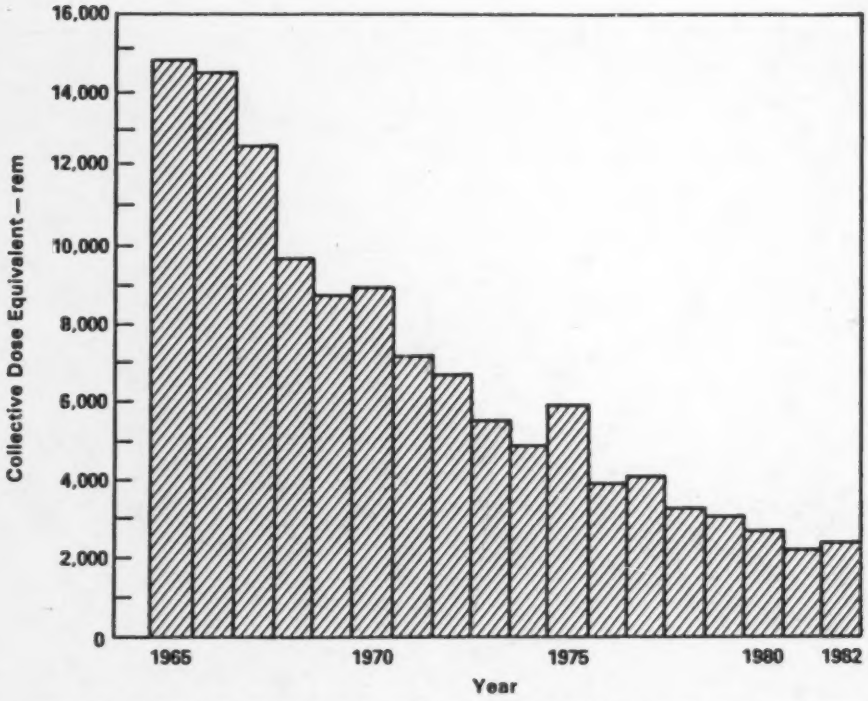


Figure 4. Total Collective Dose Equivalent for All DOE/DOE Contractor Employees Who Received an Exposure Greater Than 1 rem, 1965 - 1982

APPENDIX I

DR. ALPEN AND DR. HAYES

1. In your testimony you have described the successful applications of accelerated heavy ions to the treatment of tumors that are difficult to treat by other means.

   a) How many patients are there in this country that would require this treatment?

   Response: For diseases for which we have already demonstrated a high success rate, it is expected that the following number of new patients per year would be candidates for therapy:

Pituitary disease	200-300 per year
Eye Melanoma	600 per year
Spinal Cord and brain	300-400 per year
Brain vascular disease	1000-1500 per year
TOTAL	2100-2800 per year

   b) How many patients a day can you treat?

   Response: With our present facilities we can treat about 10-12 patients per day. The usual scheme of treatment calls for twenty treatments over a 4 week time span. That means we can admit about 2-3 new patients per week. On the present operating schedule this would amount to about 100-150 new patients per year under optimum conditions.

   c) Is there a need for additional facilities?

   Response: From comparison of the numbers above, the need for an additional facility is obvious. We are particularly concerned that as pressure mounts for treatment of diseases for which we have proven success, there will be very little time for research on new therapies that might be successful. The latter is, after all, the principal reason for the existence of laboratories such as ours.

   d) Does DOE intend to support the construction of additonal facilities?

   Response: The DOE has so far not been willing to support a new facility as a line item in their budget, but they have indicated their willingness to support such a request through the NIH. We believe that to be a serious mistake, since DOE has proven competence in building and managing large accelerator construction. NIH has historically not developed management procedures for such efforts. Of course, there is a mix of both DOE and NIH research being done on the present machine.

2. Many of the DOE programs in recent years have been badly impacted by budget cuts.

   a) What have been the principal fiscal constraints on orderly progress for your program?

Response: During the past five years there have been serious fiscal constraints on our programs as the result of cuts in the DOE budget. We have sought funding from NIH and have been successful in maintaining a sound scientific program. The funding from NIH requires enormous effort on the part of our investigators, and because of the nature of NIH grants (relatively small and not capital intensive) we have been forced to defer essentially all new initiatives.

b) How have the funding levels over the past five years influenced your programs?

Response: The level of declining dollar levels have as mentioned just above prevented the start of all new initiatives in imaging research for nuclear medicine and radiation treatment programs that require major fiscal commitments. Many exciting new ideas have thus been undeveloped for over five years.

3. The DOE remains the principal agency funding and managing research on applications in medicine and biology.

a) Should this responsibility be transferred to another agency?

Response: We believe that the DOE is still the best equipped agency to support and fund research in nuclear medicine, radiation medicine and biology. They have a sound national laboratory system which continues to do good research in spite of the fiscal constraints, and most of all, DOE management knows best how to manage large, multidisciplinary science in these fields. NIH, the only apparent alternative, operates more on the individualized reserach effort. Both these approaches are successful and commendable, but each system serves a different scientific need.

b) Has the leadership role of the U.S. community in nuclear medicine and radiation medicine declined in recent years due to diminished funding?

Response: There is no doubt at all that the U.S. community is rapidly falling out of their leadership position in nuclear and radiation medicine. The high technology portions of the work especially is moving into the Japanese sphere. In the most recent detection system built at the Donner Laboratory, all of the detectors are of Japanese design and manufacture.

UNIVERSITY OF CALIFORNIA, LOS ANGELES UCLA

BERKELEY · DAVIS · IRVINE · LOS ANGELES · RIVERSIDE · SAN DIEGO · SAN FRANCISCO SANTA BARBARA · SANTA CRUZ

DIVISION OF BIOPHYSICS
DEPARTMENT OF RADIOLOGICAL SCIENCES AND
LABORATORY OF NUCLEAR MEDICINE
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LOS ANGELES, CALIFORNIA 90024
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March 27, 1984

Mr. James H. Scheuer
U.S. House of Representatives
Committee on Science and Technology
Chairman, Sub-Comittee on Natural Resources,
Agriculture Research and Environment
Suite 2321 Rayburn House Office Building
Washington, DC 20515

Dear Mr. Scheuer:

My answers to the questions indicated in your March 15th, 1984 letter are as follows:

Question 1:

In the development of positron emission tomography to the state its at today, there must have been crucial support from a number of sources.

a. How important was the support from DOE?

b. Does DOE plan to support this research in some other fashion?

c. Are there other avenues of support that you can take advantage of?

Answer:

a. The support from DOE was critical. Positron emission tomography (PET) is a good model system for understanding how for many developments occur in nuclear medicine. PET is a technology which brings together the use of chemicals or compounds of the body with labeled radioisotopes, instrumentation development, physics, chemistry, biochemistry, physiology, mathematics and computer sciences; with the clinical specialty areas (i.e., cardiology, neurology, neurosurgery, oncology (cancer), gerintology, etc.) for the development of new research, diagnostic and therapeutic approaches to human disorders. This is in fact the definition of nuclear medicine, since it is a programmatically or problematically oriented group of individuals who develop and apply technology transfers to biomedical and clinical environments. Since technology in this field is nuclear based, it derives in large part from internal technology transfers within the greater DOE system. Thus, it represents the medical and peaceful use of radiation consistent with a Congressional Atomic Energy Act of 1946 and a more diverse and efficient use of research and development programs within the greater DOE.

However, a most critical issue is the long-term and stable commitment of DOE to nuclear medicine in order to provide these developments. It

provides a base laboratory setting and support for people from many different programs to bring their area of expertise to a common goal. The hallmark of this laboratory is the development of nuclear instrumentation and methods for which there is no other home, since the mission of NIH is to apply technologies to the study of human disorders, and not to develop them per se. NSF is a broad based program for the basic sciences but is not focused on technology in the nuclear area or technology for biomedical and clinical applications. Nuclear technology is a "base technology" of DOE.

b. The answer to this question is somewhat unclear. There have been discussions about taking our laboratory off-site and putting it in a competitive renewal environment. This is a position that has been discussed by Charles Eddington on the basis of using the peer review system to deal with the budget deficits in his division of OHER. We are not concerned with peer review since this exists now in all forms of our support and we have done very well. Our main concern is concept of an on-site laboratory. Somewhere there must be a sense of a long-term and stable commitment to allow us to hold our laboratory intact, and to recruit and retain the best faculty in the world. To understand this, it is important to separate the on-site laboratory concept from the economics. Obviously the latter is necessary but it is not sufficient to maintain a programmatic commitment.

   DOE, in the person of Alvin Trivalpiece, has been very responsive regarding the OMB statement that our laboratory budget will be zero in 1985. He stated in his testimony before the Congressional Committee on Science and Technology on March 13th, 1984 that he is hopeful about finding ways to support our laboratory. However, it still stands that there is a line item in the OMB budget setting our award to zero for 1985 that must be directly dealt with, and that OHER has about a 25 million dollar defict for the 1985 budget, due to the use of GSO money in previous years. This deficit is not apparent from the balance sheets of the presidential award because the GSO money is not shown (i.e., the presidential award shows about 180 million for 1984 when in fact the "real" budget is over $210 million).

c. We have already taken many other avenues of support. During these last two years we have used our base DOE laboratory support as leverage or matching money to acquire additional funding from NIH, National Institute of Mental Health, the private sector and commercial sources. Thus, consistent with this administration's policy, we have diversified our source of funding. However, none of this is valid without the long-term stable commitment to our DOE laboratory from which all this matching money was acquired. We are a very competitive and productive laboratory, and more than able to raise these matching monies, but I must state again that there is a requirement of base support that we obtain from DOE. At this point our support is about 50% from DOE and 50% from other outside sources. This however cannot go farther or it will erode the stability of our laboratory since the other outside money tends to be soft and cyclic. We have of course also received large amounts of support from our University in the form of space, money faculty positions and their

enthusiastic support and participation to solve whatever problems arise. We are one of the most productive and visible programs in the medical school system of the University of California.

Question 2:

The FY 1985 budget figure showed that the contract for the laboratory has been terminated.

a. How do you feel this decision will effect the progress of your research?

b. How many other people will be effected by this decision?

c. Will the laboratory as an organizational unit be able to survive this cut-back?

d. How does this cut-back influence your future plans?

Answer:

a. This decision, if upheld, would destroy our laboratory. We lead the world in the technology development and application of positron emission tomography simply because we have the best collective group of people in this field. Without the security of long-term commitment of our laboratory, our faculty would disperse. In fact, all of the outside monies that we have obtained have been based upon matching monies from DOE and thus this would be invalidated. Our faculty and staff are our greatest resource and this would be lost.

b. Our laboratory has a direct employment of about 50 people for which DOE funds are the overwhelming source of faculty and staff salaries, and they would all be affected by this decision. We are not a university department that has adjunct support from DOE. This is our principle means of financial support. In addition, there are about 50 people in other departments that work with us in cooperative programs that would be severely affected. In addition, since we are the leading lab throughout the world in positron emission tomography, we play a seminal role in the development and application of the technology for all of these labs. The majority of the other labs throughout this country (i.e., Harvard, Cornell, Duke, University of Pennsylvania, NIH, Johns Hopkins, University of Florida, University of Wisconsin, Washington University, University of Chicago, and several others), along with those in Canada, Europe and Asia have been set up during the last five years to apply this technology and depend heavily upon DOE labs such as UCLA, Donner Lab, Brookhaven and Oakridge for basic technology development. This synergistic relationship is critical to the development, application and disseminaton of this technology. Destruction of this programmatic commitment at this early critical stage in the development and growth of PET would have far reaching and long-term implications.

c. As discussed above, the organizational units of the laboratory will not survive if our base DOE laboratory concept and support are taken away.

d. My future plans would become very uncertain. It is not that I or the other people in this program would go without jobs. They are a very distinguished and scholarly faculty who will have no trouble finding new positions. The issue is that this cut back will have destroyed the development of a technology that if its full potential can be realized, will have a major impact on biomedical human research, the discovery of the biochemical basis of human diseases and the development of more specific and effective treatments.

Question 3:

In your research on brain disorders, have you been able to probe the inner most workings of this vital organ?

a. What has been the impact on health care of this technology?

b. How has it helped to better peoples lives?

c. Do you foresee future developments leading to an even better understanding of brain function?

Answer:

a. At this point in time, positron emission tomography is in a developmental stage, so it has had little impact on the health care system. However, no one would argue with the fact that any technology that provids a way to watch and measure the body chemistry in the living human subject would be one of the greatest developments in medicine of this century. All of the functions performed by the human body have a chemical basis and all human diseases are of a chemical origin. Thus, the earliest and most specific diagnosis, the basis for developing new and more effective treatments and evaluating response to therapy will be by chemical means. There is no technology that we know of today that offers more promise for the fulfillment of this objective than positron emission tomography. Thus the impact and benefit of this technology is best represented by an investment in a better future.

b. This has been described previously in my testimony before your committee and also in the written document that I provided at the time of the hearing.

c. There is no question that this technology will provide us more information and knowledge than has ever existed in the past regarding the human brain. We are in an era of brain research that is advancing at an incredible rate. However, it should be recognized that the overwhelming majority of this work is occurring in animals and PET provides a bridge for the expression of this new knowledge and understanding to the human subject. The major hallmark of the brain research era we are now in is understanding the chemical basis of human behavior and the alterations that result in symptomatic changes that reflect underlying disease. No other technology can provide a direct chemical assessment of this in the

subject. In addition, about 25% of the human brain is in fact unique to the human and does not exist in animals. This is the frontal cortex which is the area of the human body that differentiates us to the largest degree from other animals. It is of course also believed to be the center of mental health and behavioral disorders. Thus, eventually, studies must be performed in humans.

I extend the appreciation of all members of our DOE Laboratory and those inside and outside the University of California who support and believe in our work, for your concern and help in maintaining and advancing our laboratory as an important resource of this country. If I can be of further help please feel free to contact me.

With personal regards,

Michael E. Phelps

Michael E. Phelps, Ph.D.
Jennifer Jones Simon Professor
and Chief, Division of Biophysics

MEP/mk

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Office of the Director

4 April 1984

Dr. James Greene
Subcommittee on Natural Resources,
Agriculture Research and Environment
Committee on Science and Technology
Room 388, House Office Building - Annex No. 2
U. S. House of Representatives
Washington, DC 20515

Dear Dr. Greene:

This letter is in response to Congressman Scheuer's letter of 15 March.

Question 1A. Although radiation-induced cancer is a relatively rare event even in the exposed Japanese, it must be remembered that, although the dose to a few individuals was in the hundreds of rads, the average dose on which the overall induced cancer rate depends was relatively low--perhaps 15 or 20 rads. A good part of the reason that radiation-induced cancers are rare events in most human populations is that the overwhelming majority of us are exposed to only very small doses (see also the answer to Question 1C, below). Moreover, the chance of developing cancer depends not only on the radiation dose but probably on genetic factors (mostly unknown) that control repair systems or the rate of expression of neoplastic cells. Such ameliorating factors are not well understood but they probably play important roles not only in radiation-induced cancer, but in other cancer causation, e.g., a relatively small fraction of smokers get lung cancer, even though the experimental evidence is overwhelming that smoking is the major cause of lung cancer.

Question 1B. The sources of low levels of radiation that human beings might be exposed to are estimated in a National Academy Report entitled "The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980" (BEIR III). Background radiation coming from cosmic rays, terrestrial radioactivity and radioisotopes incorporated naturally in our bodies amount to approximately 100 mrems per year (0.1 rem per year). In addition, medical procedures using x-rays and radioisotopes for diagnostic procedures account for approximately another 100 mrem per year to the average person in the United States.

Question 1C. The data on cancer risks from environmental sources are summarized in an article by Doll and Peto in the Journal of the National Cancer Institute, 66:1191-1308, 1981. Their estimates based on linear extrapolations from high doses and dose rates indicate that in the United States background radiation could account for approximately 5500 cancer deaths per year (page 1254), medical diagnostic procedures could account for approximately 2000 cancer deaths per year (page 1252), and occupational exposure and exposure of the general population to air pollution, in particular, that arising from global fallout could account for approximately 700 cases per year (pages 1245 and 1248). Thus, approximately 8000 cancer deaths per year could be ascribed to ionizing radiation. This number represents approximately 2% of the total cancer mortality. This may seem small, but it is worth realizing that this number is appreciably greater than the approximately 5000 deaths per year from malignant melanoma. In part, the overall frequency of cancer deaths from ionizing radiation is very low because, as noted above, the exposure to the average person in the United States is low. Nevertheless, increases above this level would be expected to increase the cancer mortality rate. There are three important reasons why continuing support is needed of research on the low level effects of ionizing radiation exposure (one must remember that purely epidemiological studies on human populations will not tell us what the low level effects are because of, in addition to statistical problems, the large variabilities in the life style and exposure of the average populations).

1) Ionizing radiation is one of the best environmental agents for the development and testing of models for carcinogenesis resulting from physical or chemical agents. The dosimetry is excellent compared to that for chemicals, and the molecular mechanisms by which ionizing radiation produces effects are rapidly becoming better understood, especially with the recent advances in DNA sequencing and genetic engineering. Hence, it should prove possible, by combining molecular data with cellular and animal data, to make good theories--as physics now does--that permit us to extrapolate and to obtain dose response curves at all radiation doses. Such curves could represent superior models for hazard estimation, not only for ionizing radiation but for chemical carcinogens in the environment. It is important to have estimates of such hazards for practical reasons. For example, what has been the hazard to individuals exposed to the radiation from radioactive steel entering the United States from Mexico?

2) Public Law 97-414, known as the "Orphan Drug Act", requires among other things, that the Secretary of Health and Human Resources "devise and publish radioepidemiological tables that estimate the likelihood that persons who have or have had any of the radiation-related cancers and who have received specific doses prior to the onset of such disease developed cancer as a result of these doses". The tables developed should show a probability of causation of developing such radiation cancers associated with the receipt of doses ranging from 1 mrad to 1000 rads, stratified by sex, age at the time of exposure and time from exposure to the onset of cancer in question. The numbers in such tables may be used to estimate the compensation to be given to

individuals exposed to ionizing radiation as a result of their occupation (for example, veterans of the Armed Forces) or inadvertant exposures from radiation sources or radioactivity releases. The principal point is that if we cannot make predictions for ionizing radiation we will not be able to make them for any other environmental hazard. Thus future legislative and legal action may well be based more on hand waving rather than scientific facts.

3) A further example involves hazard versus benefit, as in mammography screening programs for breast cancer. In the United States, mammography probably represents the most widespread exposure of the breast to repeated doses of low levels of ionizing radiation. Hence, it is important to know quantitatively the hazards of the procedure compared to its benefits.

Question 2A. The support for our unique national facilities used in Structural Biology (the High Flux Beam Reactor, HFBR, the National Synchrotron Light Source, NSLS, and the Scanning Transmission Electron Microscope, STEM) is in two parts--operating money for personnel and supplies and capital money for the construction and purchase of the necessary state-of-the-art instruments to be used with these large facilities. The HFBR and STEM have been in existence for a number of years and are operational. The NSLS should be operational in a month or so and fully operational in another year. The major present shortfall in funding is in the equipment budget, but when the NSLS becomes operational there will be a large shortfall in personnel funding, which will affect seriously our abilities to help outside users in universities and other research institutions to do investigative work using these facilities.

Question 2B. Structural Biology is able to function at present. Our concern is that we will not be able to construct the necessary instruments to use with these facilities and, in future years, provide the staff to help outside users from universities and industry.

Question 2C. Similar efforts in the development of such facilities are being made in Japan and in the European Molecular Biology Organization Laboratories. If the Laboratory gets the needed instrumentation, its capabilities will be ahead of Europe in the STEM and NSLS area, and, in the reactor area, about equivalent to the efforts in Grenoble, France. Without money to help users and construct or purchase the necessary instrumentation, the Laboratory will fall behind.

Question 2D. In calendar year 1983 there were 94 outside scientists using the unique facilities (the total department staff is 114). These outside users worked on approximately 47 projects. When the NSLS becomes fully operational and the hoped-for expansion at the HFBR and the STEM takes place, we expect the number of projects per year to increase by 4 to 5 fold. Hence, the number of outside university and industrial scientists using our facilities would increase to over 400 per year. Our existing staff could not take care of this large number, even if they neglected completely the necessity to do research of their own and develop new instruments to make the facilities competitive on a world-wide basis.

Question 3A. The BEIR III report indicates that the difference between the various types of dose response curves at low doses amounts to a 2 to 3 fold effect between the linear and the linear quadratic functions. The estimates using a quadratic function differ from (are lower than) the linear, by almost a factor of 20. In general, the differences between the various formulations increase as the dose decreases.

Question 3B. The differences are significant in 3 areas: 1) estimation of the probability of causation of cancer from known radiation exposures, 2) the setting of acceptable radiation exposure limits for occupations as well as for the general public, and 3) the setting of occupational exposure limits for workers in space. The latter is not a serious problem now but could be if space stations are constructed in the future. For example, the National Research Council Report, "Electric Power from Orbit: a Critique of a Satellite Power System" in 1981, pointed out that the predicted excess cancer mortality in space workers exposed to the ionizing radiation environment in geosynchronous orbit associated with a reference design of a solar-powered satellite could be as high as 10%. This is a risk much greater than that experienced in other occupations. Clearly, an error in the wrong direction in this estimate would be serious for space workers.

Question 3C. Yes, however, the extrapolation can be simplified by working with some well-understood biological systems that can be examined at low doses. Epidemiological data on human beings is of limited use in this regard.

Question 3D. Within factors of approximately 3, we can predict at least upper limit risks from external low-energy transfer radiation. The risk estimates from neutrons are much less certain, as are those from ingested radioisotopes.

Question 3E. The extent of our understanding of the action of radiation on biological systems is based to a very large extent on research supported by DOE/OHER, involving all levels of biological organization. The following quote is taken from Seymour Jablon, in Radiation Carcinogenesis: Epidemiology and Biological Significance, (Boice and Fraumeni, Jr., Eds., Raven Press, 1984, p. 8), "If being embodied in legislation is a sign of maturity, then radioepidemiology, as the Senate bill calls it, is a mature science. We who work in this field are well aware of how much we do not know, how imprecise are some of the numbers we draw from data that we wish were bigger and better. Nevertheless, in a sense, the epidemiology of radiation carcinogenesis has come of age--we can begin to return useful answers to important public question."

Sincerely yours,

V. P. Bond

V. P. Bond, M.D.
Associate Director

jal

QUESTIONS FOR DR. BOND

1. ON PAGE 4 OF YOUR TESTIMONY YOU STATE THAT THE INCREASE IN OVERALL CANCER RATES FOR THE JAPANESE ATOMIC BOMB SURVIVORS IS LESS THAN ONE PERCENT, AND THAT THEY RECEIVED HIGH DOSES IN A SHORT TIME, WHICH IS MORE HAZARDOUS THAN LOW DOSES OVER LONG TIMES.

   A. DOES THIS SURPRISINGLY LOW FREQUENCY OF INCREASED CANCER SUGGEST THAT RADIATION INDUCED CANCER IS A RELATIVELY RARE EVENT IN HUMANS?

   B. WHAT ARE THE SOURCES OF LOW LEVELS OF RADIATION THAT HUMANS MIGHT BE EXPOSED TO?

   C. WHAT ARE THE CANCER RISKS ASSOCIATED WITH THIS EXPOSURE AND HOW DO THEY JUSTIFY CONTINUING SUPPORT OF RESEARCH ON LOW LEVEL EFFECTS OF IONIZING RADIATION.

2. ACCORDING TO THE IMPACT OF THE FY 1985 BUDGET ON YOUR LABORATORY'S RESEARCH PROGRAM, PRESENTED AS A TABLE AT THE END OF YOUR TESTIMONY, THE SUPPORT FOR THE NATIONAL FACILITIES FOR STRUCTURAL BIOLOGY IS ONE THIRD OF WHAT IS NEEDED.

   A. HOW DOES THIS LOW LEVEL OF FUNDING EFFECT THIS PROGRAM'S FUTURE?

   B. IS THIS PROGRAM CURRENTLY ABLE TO FUNCTION AT ALL?

   C. ARE THERE SIMILAR EFFORTS TO DEVELOP SUCH FACILITIES BEING MADE AT LABORATORIES IN OTHER PARTS OF THE WORLD AND ARE WE IN DANGER OF FALLING BEHIND IN THIS EFFORT?

   D. HOW MANY OUTSIDE SCIENTISTS A YEAR WOULD BE EXPECTED TO USE THE FACILITIES?

3. ON THE SUBJECT OF LOW LEVEL RADIATION EFFECTS,

   A. HOW BIG IS THE DIFFERENCE AT LOW DOSES BETWEEN THE VARIOUS TYPES OF DOSE-RESPONSE CURVES, (I.E. LINEAR VS. LINEAR-QUADRATIC) AND DOES THIS DIFFERENCE INCREASE AT VERY LOW DOSES?

   B. HOW SIGNIFICANT IS THIS DIFFERENCE IN TERMS OF THE ECONOMICS THAT IS INVOLVED IN ESTABLISHING A SAFE ENVIRONMENT?

   C. DO YOU AGREE WITH OTHERS WHO SAY THAT LOW LEVEL RADIATION OF MAN CAUSES EFFECTS THAT CAN ONLY BE ESTIMATED BY EXTRAPOLATING FROM HIGH DOSES AND INVOKING THEORIES THAT RELATE STRUCTURE TO FUNCTION?

   D. TO WHAT EXTENT CAN WE SAY THAT WE UNDERSTAND THE RISKS FROM COMMON FORMS OF RADIATION EXCEPT FOR NEUTRONS?

   E. TO WHAT EXTENT IS THIS UNDERSTANDING BASED ON DOE/OHER SUPPORTED RESEARCH?

Answers to Questions from HST
Subcommittee on Natural Resources,
Agriculture Research and Environment
Dr. Warren K. Sinclair, NCRP

1. YOU STATE ON PAGE 2 OF YOUR TESTIMONY THAT MANY IMPORTANT UNRESOLVED SCIENTIFIC PROBLEMS LIMIT OUR CONFIDENCE IN THE LEVELS WE FEEL NEED TO BE APPLIED FOR ADEQUATE PROTECTION FROM IONIZING RADIATION.

   A. HOW SERIOUS A THREAT IS RADIATION IN OUR LIVES AND HOW MANY DEATHS EACH YEAR FROM CANCER ARE ACTUALLY RADIATION RELATED?

   Numerically we cannot be certain <u>any</u> deaths from cancer are actually radiation related because if these occur, they are indistinguishable from those that are not radiation related. However, we must presume from exposures of limited numbers of people at higher doses that deaths also occur, but less relatively, at lower doses. For example, we must presume that the average background <u>radon</u> levels in the U.S.A., namely about 0.2 WLM/yr are responsible for 0.2% of deaths whereas the risk of dying of lung cancer from natural causes, for nonsmokers, is about 1%, i.e., indoor radon <u>may</u> be responsible for about 1/5 of the lung cancer deaths in nonsmokers, which amounts to several thousand per year. The other background radiation sources may also cause other types of cancer, but fewer deaths are likely to result than from radon.

   B. DO THESE DEATHS ALL OCCUR IN THE OCCUPATIONAL CATEGORY AS SHOWN IN VIEWGRAPH 3?

   Viewgraph 3 shows doses, not deaths. Viewgraph 4 compares <u>doses</u> not deaths, from different sources and even the average radon dose is at least as high as the average occupational dose. Average occupational exposures are low and occur to only 600,000 people instead of the entire U.S. population of 235 million and therefore, very few deaths could be presumed to result from occupational exposure.

C. WHAT CAN YOU SAY ABOUT THE ADEQUACY OF EXISTING RADIATION PROTECTION REGULATIONS?

Existing radiation protection regulations, for occupational exposure, result in average exposures which seem to be less than, or comparable with, some background sources and therefore, seem reasonable. The maximally exposed worker, if indeed any exist who could be exposed at the maximum every year for a lifetime may face a less reasonable risk and some consider there is a need to limit lifetime risk either by a lifetime dose limit or an accumulation formula.

2. YOU MENTION ON PAGE 2 OF YOUR TESTIMONY THAT THE JAPANESE POPULATION EXPOSED AT HIROSHIMA AND NAGASAKI REPRESENT IMPORTANT SOURCES OF EPIDEMIOLOGICAL DATA.

A. WHAT IS THE SIZE OF THE DATA POOL YOU ARE DRAWING UPON IN THESE STUDIES?

About 82,000 people exposed.

B. WHAT NUMBER OF JAPANESE SURVIVORS ARE DYING OF CANCER EACH YEAR IN RESPONSE TO THE RADIATION THEY RECEIVED?

A total of about 90 excess cases of leukemia and about 160 cases of excess tumors other than leukemia that are believed attributable to radiation, have died so far. At the present time, between about 10-20 excess deaths occur per year.

3. AT LAST YEAR'S HEARING, DR. GREISEMER STATED THAT IT WOULD COST $3 BILLION IF RADIATION PROTECTION LEVELS HAD TO BE LOWERED.

A. DO YOU HAVE SIMILAR NUMBERS THAT INDICATE THE ECONOMIC BURDEN OF PROVIDING ADEQUATE RADIATION PROTECTION TO WORKERS IN THE NUCLEAR INDUSTRY?

This was answered orally at the time of the hearing.

B. DO YOU ENVISION THAT RESEARCH WILL PROVIDE INFORMATION THAT EVENTUALLY WILL ALLOW LEVELS TO BE RAISED AND DOLLARS SAVED?

Research will undoubtedly contribute a great deal to our ability to make judgments in this area. It is more likely that new more restrictive

levels, which are costly, will be shown to be unnecessary, thus saving dollars, than that levels will be raised as a result of research. The EPA has already been proposing unnecessarily restrictive standards for emissions.

C. IS THERE A NEED TO IMPROVE COMMUNICATION BETWEEN THOSE PROPOSING TO DO RESEARCH ON RADIATION CARCINOGENESIS AND THOSE INVOLVED WITH PROTECTING WORKER'S LIVES?

I doubt it. Through organizations like the NCRP, professional contacts between those engaged in radiation carcinogenesis and those responsible for worker protection are fairly good.

4. ON PAGE 4 OF YOUR TESTIMONY, YOU INDICATE THAT THE GREAT MAJORITY OF THE INFORMATION YOU USE TO PRODUCE REPORTS RELATING TO RADIATION PROTECTION, COMES FROM STUDIES SUPPORTED BY THE DOE/OHER.

A. WHAT OTHER SOURCES OF INFORMATION ARE AVAILABLE THAT YOU CAN DRAW UPON?

1. The literature relating to studies supported by NIH, but often these are by the same people who have both DOE and NIH support.

2. The European and other literature sources cited by UNSCEAR. By and large, all other sources are no more than equal to the U.S.A. effort.

B. HAVE YOU BEEN AWARE OF A DECREASE IN EMPHASIS ON RADIATION CARCINOGENESIS STARTING ABOUT 10 YEARS AGO WITH THE INCREASE IN SUPPORT FOR FOSSIL FUEL RESEARCH?

Yes. In general it is clear that funds once designated for radiation carcinogenesis were required to encompass studies on carcinogenesis from other energy forms and in declining amounts for a broader scope!

C. COULD PROGRAMS SIMILAR TO THOSE CURRENTLY SUPPORTED BY DOE/OHER BE CONDUCTED AT UNIVERSITIES INSTEAD OF NATIONAL LABORATORIES?

Some could, but most could not because the national laboratories were set up with special facilities to do just that. The Janus Reactor at Argonne is a good example--it was set up to provide an exposure chamber to neutrons for 500-1000 mice at a time. Not only is this special in its

nature (to say nothing of the backup animal housing required) but reactors are better operated in the remote, but experienced laboratory environment in which reactors are normal and not strange beasts. These arguments and further examples could be extended more or less indefinitely.

D. WHY IS IT IN OUR OWN NATIONAL INTEREST TO MAINTAIN A STRONG POSITION IN MATTERS OR RADIATION PROTECTION?

The U.S.A. has, willy-nilly, acquired a leadership role. It developed atomic energy in the Manhattan District in the form of the first chain reaction and developed the only two bombs ever used as weapons, led the world in the development of power reactors and breeder reactors (the latter incidentally is about to be stupidly thrown away!). Thus, it is incumbent on the U.S.A. to have a concomitant lead in the safety aspects of the problems they have done more than anyone else to generate. Furthermore, the U.S.A. has a general approach to worker and other safety second to none in the world and since radiation protection is inevitably involved with other levels of occupational safety--and is no longer uniquely better than many other occupations--it is necessary to preserve the highest standards, or forget about our lead role in this or in any other field.

1. ON PAGE 11 OF YOUR TESTIMONY YOU MENTION ESTABLISHING A USERS FACILITY FOR BIOPROCESS RESEARCH.

   A. WHAT CONTACTS HAVE YOU MADE WITH UNIVERSITY AND INDUSTRIAL FIRMS TO ENSURE THAT THERE IS A NEED FOR SUCH A USER FACILITY IN EAST TENNESSEE?

   During the past three years the Oak Ridge National Laboratory has had extensive discussions as well as cooperative research arrangements with approximately 20 universities throughout the U.S. and half a dozen private firms relative to the components of the proposed Bioprocess Research User Facility. More recently, because of increasing interest in this field, more targeted negotiations have occurred involving the University of Tennessee, Martin Marietta Corporation and East Tennessee firms to develop longer-term synergistic plans in biotechnology (including bioprocess research and development).

   The development of the Technology Corridor between Oak Ridge and Maryville, Tennessee, in which several industries in biotechnology are emerging, adds another dimension to the need for such a user resource facility that can serve as focal point for universities and industry while simultaneously advancing the state-of-the-knowledge in this highly important research area.

   B. HOW MUCH BUDGETARY SUPPORT DO YOU THINK IT WILL TAKE TO ESTABLISH SUCH A FACILITY AT OAK RIDGE?

   The proposed Bioresearch User Resource would not require the specific allocation of additional budgetary support. The proposed bioprocess research users resource would combine currently existing activities and resources from the Biology Division located at Y-12 and the Chemical Technology Division located at X-10. There currently exists program element funding from several parts of DOE and other sponsoring organizations. Except for incidental costs incurred by visiting scientists from other universities or private industry, the costs would be borne by the users. We are planning a new programmatic initiative, Protein Engineering, that will complement the concept and functions of the Bioprocess Research User Resource.

   C. TO WHAT EXTENT WILL THIS EFFORT DRAIN FUNDS AWAY FROM PROGRAMS ALREADY IN EXISTANCE?

   We do not anticipate that this effort would drain funds away from programs already in existence. Rather, we would anticipate that the core users resource would provide unique, or rare, resources to our scientists working in concert with visiting scientists from other labs, universities or private industry.

2. RECENTLY, WE'VE HEARD FROM THE CURRENT ADMINISTRATION THAT LONG-TERM, HIGH RISK RESEARCH IS WHERE THE GOVERNMENT SHOULD BE SPENDING ITS MONEY.

A. ARE YOU EMPHASIZING ANY RESEARCH OF THIS TYPE AT OAK RIDGE?

Yes, we are emphasizing long-term, high risk research at Oak Ridge. In fact, our work has been and continues to be comprised of both short-term and long-term studies, some of which are more basic or fundamental while others are more targeted or applied. Both components are needed for successful research programs and it is the mix of these components that is difficult for a research manager to balance and plan for.

Over the years there have been shifts in federal policy as regards the relative mix of short-term versus long-term components. Sometimes, depending on the specific administration or the science policy being pursued at that time, one component might be preferred over the other. My personal preference is to have a healthy portion of the long-term, high risk research included in the overall research program. There is room for growth in the long-term component. This approach tends to maximize the interdisciplinary team research effort using dedicated or unique (perhaps rare) resources that exist at the multiprogram national laboratories. Another important component of this mix, institutional memory, is important when one is pursuing long-term programs requiring much data acquisition, analysis, and transfer to other communities such as the private sector or academic groups. One example is the continuity required for global environmental problems that have truly long-term research components. On the other hand, organizations other than multipurpose laboratories are often in a better position to conduct short-term research not generally requiring the components mentioned above. Again, I don't think it is a question of either or, but rather a question of the relative amounts.

B. DO YOU SEE EVIDENCE THAT SUPPORT IS EASIER TO GET FOR THIS TYPE OF RESEARCH?

It may be too soon to make an informed judgment as to whether or not support is easier to get for long-term, high risk research because it takes some time to shift the existing programs to the revised or new programmatic guidance received from DOE or other sponsors of research. I do see evidence, for example from planning exercises both at ORNL and in DOE, that the research programs in many cases are in a state of transition and moving toward a research mix that will emphasize more of the long-term, high risk research component. It is important to point out, however, that the long term, high risk research can be planned and managed more efficiently, if multi-year funding is available as I delineated in my written testimony.

C. WHAT IN YOUR OPINION ARE SOME EXAMPLES OF LONG-TERM, HIGH RISK RESEARCH THAT DOE/OHER SHOULD BE SUPPORTING?

Some examples are given below.

- Advanced biomonitoring techniques (e.g. see the mixed function oxidase system given in Appendix B of my written testimony.)
- Chemical dosimetry needed to better understand the relation between exposure and biological effect for chemicals.
- Development of practical methodology, instruments and programs for worker protection in developing energy technologies.
- Understanding mechanisms of interactions, at the cellular and molecular level, between biological components and effects.
- Understanding mechanisms of repair for biological structures that are damaged by chemical or physical agents.
- Increasing our knowledge of the biogeochemical cycling of elements, popularly known now as acid rain (sulphur, nitrogen) and the greenhouse effect (carbon dioxide).
- Work on the long-term aspects of chemical waste handling, storage and disposal (e.g. using biological systems, recycling, conversion, chemical alteration or better disposal methods).
- Exploitation of molecular and cellular systems to detect and measure effects of low-level exposures to radiation and energy-related chemicals on people and ecosystems.
- Development of nuclear medicine techniques and continue to transfer this research information to the private sector.
- Instrumentation for detecting and quantifying radiation and chemicals in the workplace or in the environment.

3. ACCORDING TO THE ENERGY RESEARCH ADVISORY BOARD'S RECOMMENDATIONS MADE IN APPENDIX D, OF YOUR TESTIMONY, YOU HAVE THE TASK OF SUSTAINING SCIENTIFIC STAFF CAPABILITIES AND RESEARCH FACILITIES AT YOUR INSTITUTION.

   A. HOW MUCH STAFF HAVE YOU BEEN FORCED TO LET GO SINCE 1981?

   If we look specifically at the number of people lost as a result of budget shortfalls resulting from OHER sponsorship during the period FY81 through FY83, we find that 146 people were lost from the Biology Division. One then needs to add the impacts of these reductions on the supporting activities throughout the Laboratory. This accounts for another possible 73 individuals bringing the total personnel impact caused by the budgetary shortfall from the OHER program within the Biology Division during this period to 219 persons within ORNL.

   Not all these people were "let go" as some were placed in jobs in other parts of the Oak Ridge National Laboratory or other nuclear division installations. We also assisted people in securing employment outside of the Oak Ridge complex. However, these people were lost from the ORNL biomedical-environmental program.

   The impact on the ORNL Biomedical and Environmental Sciences research program supported solely by DOE/OHER can also be examined for the period FY82 through FY83. For these two fiscal years, we lost DOE/OHER funding comparable to support for about 75 people in the impacted research divisions. Two-thirds of these research and support personnel were in the Biology Division, 20% in the Environmental Sciences Division and the remaining 14% in other units conducting DOE/OHER funded research.

   An additional 35 ORNL support and services personnel were impacted by the reduction of the 75 person loss in the research divisions bringing the ORNL lab-wide total to about 110 people.

   B. WHAT PERCENTAGE OF LAB SPACE HAS BEEN REDUCED?

   The reduction in lab space to date has been restricted to the Biological Component of our research program. The reduction in the Biology Division complex during the past several years has been about 30%.

   C. WHAT UNIQUE FACILITIES HAVE BEEN DISMANTLED?

   One structure housing our comparative toxicity research laboratory has been vacated. Because of this, much of our work related to estimating health effects from comparative studies using the Ames technique and other systems, including human cells, has been discontinued or dispersed among other research units. This loss happens, sadly, at a point in time when our (and DOE's on a larger

scale) results and planning suggests the transition from short-term to long-term studies in support of energy technologies designed to produce liquid or gaseous fuels from coal or shale. Unfortunately, the transition and future of that work is in doubt.

We have also closed a building housing a radiation source used for radiation biology studies.

Major space reductions were made in the main biology building because of reduction in staff and to reduce utility costs. A unique animal facility designed to conduct experiments using mice under extremely clean conditions (a barrier facility) is no longer in use. Work for DOE and other agencies has been and could be done in these facilities.

D. DO YOU BELIEVE, THAT THE ABOVE ACTION CONSTITUTES A VIOLATION OF THE "NATIONAL TRUST" MISSION WHICH YOU REFER TO IN APPENDIX D OF YOUR TESTIMONY?

I personally believe that the serious impact of reduced budgets for the DOE's Office of Health and Environmental Research is leading to a situation where this "national trust" mission may indeed be in jeopardy of being violated. The impact has been greatest for the biological components of the program. The Energy Research Advisory Board specifically mentioned the "national trust" mission with respect to certain research areas that include nuclear medicine and radiation biology. I believe the former is being progressively weakened and the latter has been seriously compromised during recent years because of reduced funding. Incidentally, the latter is occurring at a time when there is a pressing need for research programs to supply answers in neutron radiobiology and dosimetry. There also needs to be interagency mechanisms for coordinating radiation research. Two organizations (the Interagency Radiation Research Committee and the Radiation Policy Council) with interagency coordinating responsibilities have been in place for several years but are now defunct. I believe something needs to be done to correct this situation.

4. ACCORDING TO YOUR TESTIMONY ON PAGE 12, IT APPEARS THAT IF THE FY '85 BUDGET REQUEST IS APPROVED WITHOUT AMENDMENT, THEN THE OHER PROGRAM MAY BE IN JEOPARDY.

A. DO YOU BELIEVE THIS COULD HAPPEN IN THE COMING YEAR IF STAFF LEVELS AT THE LABORATORIES DROP BELOW THE CRITICAL MASS?

Yes, I believe this a real possibility, perhaps not during FY85, but in the very near future. I understand some OHER funded laboratories are scheduled to lose base funding during FY85. These organizations obviously will be seriously impacted. Still others may drop below critical mass during FY85. If the FY85 budget request is approved without amendment, the biological research components are

most vulnerable to being placed in jeopardy at ORNL and other DOE laboratories.

B. WHAT IS THE CRITICAL MASS AT OAK RIDGE AND HOW CLOSE ARE YOU TO IT NOW?

I understand the Office of Health and Environmental Research's funding has been reduced by approximately a factor of two during the past half dozen years after one accounts for the cost-of-living changes.

As I mentioned earlier, most of the impact of the budgetary shortfall has been experienced by the biology component of the Life Sciences program at ORNL. The attached figure shows the change in personnel within the Biology Division resulting from program shortfalls from all sponsors (e.g. OHER, other parts of DOE and other federal sponsors). For the period FY 1981 through FY 1983, the level decreased from approximately 350 people to 200 people at the end of FY83. Biology Division staff levels predicted from the current FY85 budget request would be further reduced to about 150 if the requests are not amended. At this rate of change in program funding, personnel would reach zero within several fiscal years. A critical mass is required for large interdisciplinary biomedical programs. Thus the program's survival would be compromised before FY 1987.

C. WHAT NATIONAL NEEDS WILL GO BEGGING IF THERE IS A COLLAPSE OF THE PROGRAM DUE TO BUDGET RESTRICTIONS?

Several examples can be cited. The important research component of our national nuclear medicine program could be lost. This program has contributed much to the private business communities that provide these diagnostic and therapeutic medical techniques that significantly improve the quality of life for many Americans and those in other countries.

The loss of an important piece of the national research effort in radiation biology would be lost. The output of these efforts feed into the nuclear medicine and radiation protection domains.

A major impact would be on the only major national program addressing the question of assessing potential health and environmental impacts or detriments from energy producing or consuming technologies. DOE has a good record of approaching these issues from the standpoint of long-term research. Other agencies do not have the mandate or resources to fulfill this mission.

APPENDIX II

STATEMENT OF THE

SOCIETY OF NUCLEAR MEDICINE

AND

AMERICAN COLLEGE OF NUCLEAR PHYSICIANS

FOR THE

HOUSE SUBCOMMITTEE ON NATURAL RESOURCES,

AGRICULTURE RESEARCH AND ENVIRONMENT

OF THE

HOUSE SCIENCE AND TECHNOLOGY COMMITTEE

CONCERNING THE

DEPARTMENT OF ENERGY'S FISCAL YEAR 1985 BUDGET

MARCH 13, 1984

36-326 O - 84 - 18

The Nuclear Medicine community appreciates this opportunity to provide information concerning the important and vital contribution made by the Nuclear Medicine Applications portion of the Department of Energy's Biological and Environmental Research Program to the clinical practice of Nuclear Medicine.

This statement is being submitted on behalf of the Society of Nuclear Medicine and the American College of Nuclear Physicians. Both organizations strongly support the need for continued funding of Nuclear Medicine research through DOE. The College is a professional organization representing more than 1,200 physicians and scientists actively engaged in the practice of Nuclear Medicine. The Society of Nuclear Medicine is a scientific organization of 10,000 members including physicians, physicists, chemists, radiopharmacists, Nuclear Medicine technologists, and other professionals engaged in the medical use of radioactive materials. The combined membership of these two organizations constitutes the Nuclear Medicine community of this country.

The College and Society are fully cognizant of the severe budget constraints that the Congress, and your Subcommittee, must work under in addressing FY 85 budget needs. However, it has been our experience that in the field of Nuclear Medicine the application of basic research activities leads to extraordinary health benefits and cost savings for the American public. Past research resulting from DOE's Nuclear Medicine Applications Program, designed to enhance the applications of both radioactive and stable isotopes has produced benefits which we will outline.

WHAT IS NUCLEAR MEDICINE TODAY?

In a typical Nuclear Medicine procedure, the imaging study, a very small amount of a radioactive preparation is administered by injection. This tracer may be designed specifically to concentrate in one body organ, or to be metabolized or removed from the body by a particular route. Some radioactive drugs are designed to concentrate only in abnormal tissue such as cancer cells or compromised heart muscle. Sophisticated instrumentation records the transit and images the distribution of the radioactive preparation in the body. Data derived from the examination may also be processed by computer, producing improved images and quantitative information about organ function. Organ systems, even specific clusters

of cells, routinely examined in this fashion include brain, lungs, liver, kidneys, bone, thyroid, pancreas, heart, and major blood vessels.

If the study indicates that no abnormality is present, the patient can be reassured, possibly even discharged from the hospital, and the physician can turn his attention elsewhere. If the study identifies a disease process, then the physician can proceed to the next phase of diagnosis or treatment. It should be emphasized that Nuclear Medicine diagnostic procedures are safe and painless for the patient.

Diagnostic in vitro examinations encompass certain tests in which no radioactive material is administered to the patient. Instead, a sample of some body fluid, usually blood, is collected from the patient and reacted with a radioactive reagent in a test tube. These tests are used to determine the presence of hepatitis, pregnancy, and cancer antigens, to determine the precise concentration of various hormones, vitamins and drugs, and to identify pollutants or other toxic materials in the environment. Radioimmunoassay techniques permit early discovery of tumors and matastases before they become evident clinically.

Approximately 120 million Nuclear Medicine procedures are performed each year in hospitals and outpatient facilities - - on the average two on every patient admitted.

HOW EFFECTIVE ARE NUCLEAR MEDICINE PROCEDURES?

The ACNP and SNM believe that Nuclear Medicine procedures, by improving and streamlining the diagnostic process, (1) reduce total health care expense, hospitalization time, and patient suffering by rapidly directing patient treatment and (2) provide in many areas more useful information about the patient's problems than that available from other diagnostic modalities, many of which are much more costly. Because Nuclear Medicine procedures can be used to study rapidly changing body processes, as in heart and kidney, they tell us how the body functions, as opposed to other imaging procedures such as radiography which reveal only anatomic information. With the advent of the new Medicare Prospective Payment System and other emerging cost containment methods, the cost effectiveness of most medical procedures will be carefully scrutinized. We are confident that Nuclear Medicine will fare well under this scrutiny.

Nuclear Medicine techniques are especially versatile for basic research in the chemical, biological, and physical sciences. Since techniques are similar, data in these areas are easily expanded into clinical research allowing rapid application of information from the research laboratory to clinical practice. The following are a few of many such applications, demonstrating the importance of a continuing high level of research:

(A) CARDIAC NUCLEAR IMAGING

One of the most dramatic examples of the rapid transfer research developments to the hospital is the noninvasive study of the human heart. Heart attacks kill approximately 700,000 people annually and are the leading cause of death in the United States. Almost 300,000 individuals suffer their first heart attack without prior knowledge of having significant coronary disease. Early identification of persons at risk had heretofore been particularly difficult. Nuclear diagnostic techniques developed and applied within the past four years are significantly more sensitive and less risky in identifying individuals with diseased coronary arteries (hence at risk) than are other diagnostic methods such as electrocardiographic stress testing, and much less expensive and hazardous than coronary arteriography. Positron emission tomography, developed in large part by DOE laboratories, is the only method of measuring the metabolic activity of heart muscle in a non-invasive manner.

These newly developed nuclear diagnostic methods are being applied with increasing frequency in outpatient facilities where men and women in certain high risk categories can be screened for heart disease. Such techniques are also being used to assess the extent of damage after heart attacks have occurred. Marked reduction in costs is accomplished by screening patients with these procedures on an outpatient basis, reserving the expense of hospitalization and cardiac catherterization for those patients whose findings indicate the need for further studies. Additional savings result when patients requiring further hospitalization can be transferred out of the costly intenstive care units.

(B) CANCER PATIENT EVALUATION

Another example is found in cancer-related studies. The major emphasis of Nuclear Medicine in the field of cancer has moved from the therapeutic use of radioactive materials to the use of improved imaging modalities which permit earlier detection and better staging of cancers. In addition, there is growing use of Nuclear Medicine in monitoring the therapy of cancer and early discovery of recurrent or disseminated cancer. Despite this progress, present technology cannot pinpoint very small growths and often cannot determine their nature. Therefore, these techniques need to be improved by development of more specific radioactive drugs, by exploration of more sophisticated immunologic and biochemical methodology, and by development of instruments with better spatial resolution (such as that offered by emission tomographic techniques). Research with radiolabled monoclonal antibodies is an example of a promising new approach that is being pursued.

Nuclear Medicine procedures also provide a most important means of monitoring treatment in the cancer patient, by providing information on progression or regression of the tumor. This information allows the clinician to continue or modify treatment accordingly. Among the most serious problems in cancer chemotherapy are the serious side effects that anticancer drugs produce. Such effects can often be more efficiently monitored through the use of Nuclear Medicine procedures. For example, certain cancer drugs can adversely affect the heart muscle. Nuclear Medicine methods provide a guide to therapy whereby this toxicity and the possibility of drug induced heart failure can be avoided.

(C) PATIENT TREATMENT

1. Treatment of Cancer

   Improvements in cancer therapy have come about by the development of improved radiotherapy beams, better localization of the tumor, computer-aided treatment planning, and new chemotherapy agents and regimens. Further benefits derived from the use of charged heavy particles (protons, alpha particles, and mesons) arise from better dose distributions, and impressive advantages already have been demonstrated in the treatment of benign and malignant growths in the brain. Reduced morbidity and mortality and decreased cost to the

patient are achieved from these procedures. The facilities needed for these treatments are only present at DOE National Laboratories and major research centers. Additional support is needed to develop specialized low cost accelerators dedicated for medical purposes.

2. Heavy Ion Therapy

Heavy ions are being used at the Lawrence Berkeley Laboratory for the treatment of blood vessel malformations in the brain. Approximately 10,000 Americans per year are found to have this condition which is not readily treatable surgically. These patients benefit from this new mode of treatment which has been developed with DOE support in the last two years. This program also has proceeded to the treatment of other tumors, with major new successes in the treatment of ocular and spinal cord tumors.

3. Labeled Monocolonal Antibodies

Labeled monocolonal antibodies offer the promise for the treatment of certain cancers using the specificity of the antibodies to the tumor as a way of localizing the dose. These studies in many instances are provided through collaboration between National Laboratories (Lawrence Berkeley Laboratory, Brookhaven, Los Alamos, Oak Ridge), and Universities (George Washington University, Washington University in St. Louis, University of California at Davis, University of Kentucky, and others).

(D) INSTRUMENTATION DEVELOPMENT

Important new knowledge of brain bunction in health and disease has been obtained by the use of positron emission tomography (PET) imaging. PET systems have improved in performances significantly, but resolution is still lower than can be achieved ultimately and cost is still too high for all but a few research centers. Further improvements in instrumentation are needed to resolve small structures of importance. Developments in high energy physics instrumentation need to be adapted to medical application to achieve optimal resolution and diminished cost. A five-fold decrease in cost seems realistically achievable with a two - to three - fold

improvement in resolution, given funding for instrumentation support for medical applications at the National Laboratories for the transfer of this important technology.

Since PET technology requires an on-site cyclotron and is expensive, the potential of single photon emission tomography (SPECT) is being widely explored. If perfected, this technology would be readily available widely without much additional expense, since the basic instruments are already present in most Nuclear Medicine departments. Research for instrument modification and SPECT radiopharmaceutical development is heavily dependent on DOE support.

(E) PEDIATRIC NUCLEAR MEDICINE

Further examples of the improvement in health care from research and development in Nuclear medical techniques are in the area of pediatric medicine. A Nuclear Medicine bone scan is the most effective technique for the early differentiation of bone infection from soft-tissue infection, disorders that are clinically similar but markedly different in treatment and outcome. A Nuclear Medicine liver excretion study is the only method short of exploratory surgery to differentiate blocked bile ducts from liver inflammation in jaundiced newborn infants, who tolerate surgery very poorly.

There has been much recent research emphasis on the production and diagnostic use of short-lived radionuclides. An example is the cooperative effort between Oak Ridge National Laboratory in Tennessee and Children's Hospital in Boston, which was initiated to produce an Osmium-191/Iridium-191m generator. Osmium-191, with a half-life of 15.4 days, products Iridium-191m, which has a half-life of 4.96 seconds.

This short-lived isotope permits repeated determination of cardiac function with exercise or administration of drugs, particularly important in pediatrics because children change for better or worse much faster than adults, making speed in diagnosis critical. Isotopes with short half-lives deliver much lower radiation doses to patients.

(F) AGING AND ATHEROSCLEROSIS

Nuclear Medicine provides noninvasive methods of studying changes of brain metabolism during normal aging. Of significance are the initial results of DOE supported research on Alzheimer's disease, reported just this year. A group of collaborating investigators supported in the main by the Department of Energy's high technology program on nuclear instrumentation and the National Institutes of Health have discovered an extremely vital piece of information with regard to Alzheimer's disease. A pattern of decreased glucose metabolism occurs in specific areas of the brain in patients with this disease. These patterns are distinctive, particularly when compared to the patterns seen in normal aged matched individuals as well as individuals with other forms of dementia. If these observations are confirmed, it may be possible, for the first time, to identify patients with Alzheimer's disease. Precise diagnosis of a disease must be possible before effective treatment can be developed.

In addition, through investigations of the distribution of chemicals involved in neural transmission, Nuclear Medicine studies have provided for the first time a tool for understanding whether there are changes in neural transmission associated with aging.

Atherosclerosis research has benefitted in two major areas. It is now possible using Nuclear Medicine advances in positron emission tomography and single photon tomography to evaluate the efficacy of methods of treatment for stroke and heart attacks. These advances come from developments in instrumentation physics provided through the unique capabilities of the National Labs and from new radiopharmaceuticals. For example, at present, Brookhaven National Laboratory produces the purest form of the tracer Iodine-123 for use in synthesizing compounds to study stroke. The major, and for practical purposes only, source of Strontium-82 which is needed for protection of Rubidium-82 used in imaging blood flow of the heart muscle is at Los Alamos National Laboratory. A super high resolution positron emission tomograph which will provide the capabilities for the time to evaluate metabolic activity in small regions of the brain and heart is being developed by the Department of Energy at the Lawrence Berkely Lab (Donner Lab).

(G) MENTAL DISORDERS

One of the major contributions made through collaborative work between National Labs and Universities, e.g., New York University, Cornell, and Brookhaven, is the investigation of the metabolic patterns of the brain in schizophrenia. This is still an area of great controversy; however, for the first time in centuries there appears to be a quantitative tool whereby this disorder can be studied in a systematic fashion using noninvasive techniques.

The facilities and skills at the DOE supported National Laboratories are of prime importance for the development of these procedures and for their dissemination to the user community in medical centers throughout the country.

SUMMARY OF PROMISING AREAS OF RESEARCH

a) Expanded radioisotope production efforts: to provide new radioactive materials from accelerators as well as to increase the supply of current radionuclides for radiopharmaceutical development and clinical feasibility studies.

b) Radiopharmaceutical research: to improve understanding of drug distribution and mechanisms of drug action; to increase the specificity of tracer uptake; to measure the effects on biodistribution caused by particular chemical groups; to identify and characterize drug interactions; to address problems related to biological effects of environmental pollutants; to achieve reductions in patient radiation dose by developing radiolabeled drugs having more desirable properties.

c) Stable (non-radioactive) isotope tracer development: to expand the spectrum of metabolically active substances labeled with enriched stable isotopes of carbon, oxygen, and nitrogen; to study a wider variety of clinical applications of stable tracer technology.

d) Nuclear Medicine instrumentation: to improve design and efficiency of detectors; to continue development of emission and single photon emission tomography, nuclear magnetic resonance analysis, and computer-assisted diagnosis.

SPECIAL CONCERNS

The ACNP and the SNM do request the Committee to consider three specific areas of concern regarding the Nuclear Medicine Applications portion of Biological and Environmental Research Program:

First, during the past several fiscal years, there has been an inadequate percentage of the Nuclear Medicine Applications budget allocated for capital equipment needs. In comparably high technology research areas such as high and medium energy physics and nuclear chemistry, the normal percentage of capital equipment funds to operating funds is in the range of 10-20 percent. Nuclear Medicine research requires equipment and instrumentation of similar cost and sophistication; however, during the past several fiscal years, the percentage allocated for capital equipment in Nuclear Medicine research has been in the range of four percent of operating costs. The consequence of these past allocations is the present need for upgrading of equipment for the basic DOE Nuclear Medicine research program in all of the laboratory facilities.

This problem is not amenable to a one-time remedy, particularly in view of current budget constraints, but instead will require several years of attention. Therefore, we urge the Committee to consider appropriate means for assisting DOE in the identification of past deficiencies and future needs in this vitally important area. We feel this should include a policy that will provide adequate funding for capital equipment for the Nuclear Medicine research program, with an annual increase of at least 20 percent.

Second, there is a problem associated with the stable isotope production program that concerns us. Oak Ridge National Laborabory (ORNL) is the sole domestic source of certain stable isotopes necessary for the production of radioisotopes

used in medical research, diagnosis and treatment. For example, ORNL separates and distributes stable Thallium-203 for production of Tallium-201 in heart studies and stable Tellurium-124 for production of Iodine-123, a short-lived isotope which reduces pateint radiation dose and markedly improves image quality as compared with other isotopes of Iodine. Under the existing budget, only two of the four banks of separators at ORNL can be operated. Serious consideration must be given to providing sufficient funds to permit the operation of all four separators so that present needs can be met, depleted inventories reestablished, and the increasing number of research and industrial cyclotrons supplied by these separators allowed to keep pace with increasing demand from the medical community. The products of these separations are also essential to important basic research in the non-medical sciences of physics, chemistry and geology.

Third, while we fully understand the basis for incorporation of the Nuclear Medicine Applications and Live Sciences Research budgets into the significantly larger Bilogical and Environmental Research budget category, we respectfully request that the Committee clearly identify seperately that portion of the Biological and Environmental Research appropriation to be devoted to the Nuclear Medicine Applications Program.

We sincerely thank the Subcommittee for the opportunity to submit this testimony and are prepared to answer any questions that may arise.

Respectfully,

Schuyler V. Hilts, M.D.
President
American College of Nuclear Physicians

Merle K. Loken, M.D., Ph.D.
President
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3/27/84

Mr. SCHEUER. You have been very patient with us, Mr. Mares. We appreciate your patience. It is long into the day, and we thank you very much for your testimony.

Mr. MARES. My pleasure.

Mr. SCHEUER. We will stand adjourned.

[Whereupon, at 3:58 p.m., the subcommittee recessed, to reconvene at the call of the Chair.]

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